metric polyneuropathy). Only one participant reported alcohol misuse. In conclusion, the incidence of peripheral neuropathies seems to be high among patients with acute HIV disease, although in our study the number of patients with acute disease was not very high. In the asymptomatic phase, the incidence of peripheral neuropathies was low, with a tendency to increase in the advanced stages of HIV infection. Our findings are in accord with the results of other studies[4] which showed that the development and progression of neuropathy was correlated with the progression of HIV disease. The issue of peripheral nerve disorders in HIV infection should not be neglected, as the symptoms of peripheral neuropathy may be extremely painful and debilitating and may complicate the management of HIV positive patients, negatively influencing the quality of their life.

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Focal vertebral artery dissection causing Brown-Séquard's syndrome

Vertebral artery dissection typically causes an ischaemic brain stem stroke. We report a man who presented with left sided neck pain and Brown-Séquard's syndrome localised to C1, and in whom a focal C1 ischaemic cord lesion secondary to a localised vertebral artery dissection was found using MRI.

A 47 year old machine operator was admitted as an emergency with neck pain, headache, and gait disturbance. Three weeks before admission he developed minor stiffness of his upper cervical region while decorating his home, which was relieved by ibuprofen. There was no history of neck manipulation or trauma. Two days before admission he awoke with a severe left sided pounding headache and neck ache with an associated cold sensation on the left side of his neck. He was nauseated but did not vomit. His symptoms again resolved within an hour with ibuprofen, but two hours later there followed a tingling sensation in his left index finger, thumb, and forearm spreading up to his elbow. He slept for a few hours but awoke with more generalised paraesthesiae in the left arm which spread over the next 36 hours to involve the left trunk and leg. He noticed minor gait disturbance as well as left eye pain described as "like an ice cream headache". The remainder of the history was non-contributory.

Apart from xanthelasma the general examination was entirely normal. His blood pressure was 120/80. There was minor limitation of movement of his cervical spine. Cranial nerve examination was normal. Slight spasticity was evident in the left arm and leg. Both plantars were extensor. There was decreased sensation in the distribution of C2 on the left and decreased sensation to pinprick and temperature on the right and to vibration and joint position sense on the left below this. Thus the examination was consistent with Brown-Séquard's syndrome on the left at the level of C1–2.

Biochemical, haematological, and immunological investigations were normal. Fasting cholesterol was 8 mmol/l, triglycerides 3.80 mmol/l. ECG was normal. CSF protein was 0.63 g/l, glucose 3.1 mmol/l (blood 4.3 mmol/l). There was no xanthochromia. There were three white cells and 57 red cells and no oligoclonal bands. Visual and auditory evoked potentials were normal but there were abnormal somatosensory evoked potentials from the left upper limb. A sagittal T2 weighted MRI showed an area of high signal, consistent with an ischaemic lesion, in the posterior aspect of the cervical cord at the level of C1 (figure). This was shown to involve the left posterior column and left corticospinal tract on corresponding axial cuts. T1 weighted spin echo images through the C1 region showed the typical features of an arterial dissection[1] with an eccentric rim of high signal adjacent to a residual flow void in the left vertebral artery. This periarterial collar was distinguished from adjacent fat tissue by a fat suppression sequence. He was anticoagulated with heparin and then warfarin and started on lipid lowering agents. Three months later his original symptoms and signs had resolved completely.

Vertebral artery dissection has generally been associated with head and neck pain and brain stem stroke. There have, however, been some case reports of vertebral dissection with symptoms initially suggesting cervical involvement. Giroud *et al*[2] described a woman who had intermittent pain in her right arm for five days before presenting with sudden onset cerebellar dysarthria and diplopia. A few cases seem to remain localised to the cervical cord. Dubard *et al*[3] described a cervical myelopathy secondary to a vertebral

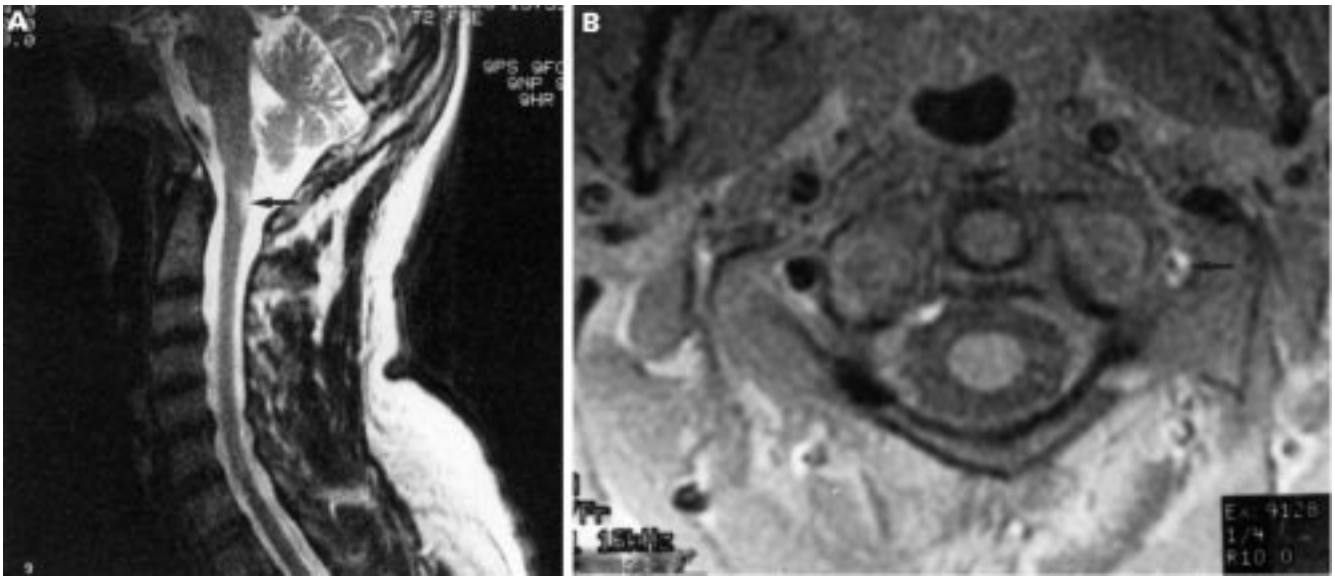

Figure (A) Sagittal T2 weighted fast spin echo sequence (TR/TE 5000/130 ms) through the cervical cord showing an area of high signal (arrow) in the posterior aspect of the cord at C1 level not associated with cord swelling. (B) Axial fat saturated T1 weighted spin echo (TR/TE 480/14 ms) through C1 shows a crescentic high signal rim (arrow) lateral to the narrowed residual lumen of the left vertebral artery as it runs though the C1 transverse foramen.

artery dissection. This may have resulted from direct compression by the dissected vertebral artery or from occlusion of a radiculomedullary artery originating from the vertebral artery. There has, however, been only one previous clinical report of vertebral artery dissection associated clearly with a lesion of the cervical cord. Gutowski *et al*[4] described a man presenting with an ipsilateral Horner's syndrome, C2 and facial anaesthesia, and posterior column loss, contralateral spinothalamic loss below T4, trapezius weakness, and hemiparesis. The cord was diffusely involved from C1 to C3. This is the level where mechanical torsion and stretch is maximal and where many dissections seem to concentrate, the dissection then spreading proximally or distally. In the present case the high signal intensity lesion within the spinal cord is consistent with an ischaemic lesion in the left posterior spinal artery territory. The posterior spinal arteries supply the posterior columns and adjacent peripheral mantle of white matter. Involvement of the posterior columns is therefore the hallmark of a posterior spinal artery infarct. It is, however, rare in its pure form and more extensive lesions with involvement of the corticospinal tracts, as in our case, are commonly seen and are due to the frequent variations in arterial supply and a complex collateral network.[5] We hypothesise that our patient had more extensive involvement or some cord swelling not seen on imaging to explain the bilateral upgoing plantars. The patient's prior decorating activities may have had an aetiological role: an association with minor and trivial neck trauma is often cited, although the true role of such everyday occurrences is hard to judge. For example, when related to chiropractic manipulation the onset of symptoms is delayed for hours or days. The evolution of symptoms in a stuttering fashion over hours or days is also typical. The nature of his retrobulbar pain is consistent with the hypothesis of referred pain being mediated by the trigeminothalamic tract in migraine and trigeminal autonomic cephalgias.

In conclusion, we draw attention to vertebral artery dissection as a cause of spinal cord ischaemia and Brown-Séquard's syndrome.

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The familial parkinsonism locus on chromosome 4 and idiopathic Parkinson's disease in Japan

Parkinson's disease is the most common neurodegenerative disorder after Alzheimer's disease, preferentially affecting locomotor activities of elderly people. Although our knowledge concerning the pathogenesis of Parkinson's disease is still limited, some environmental toxins have been postulated as candidate substances which accelerate dopaminergic neuronal death through impaired cellular metabolism, such as mitochondrial oxidative dysfunction or excessive effects of free radicals. However, there has been increasing evidence suggesting that genetic factors may play some part in the pathophysiological processes of this disease. For example, studies using PET indicated a significantly higher concordance rate for decreased striatal [^{18}F] dopa uptake in monozygotic twins.[1] Furthermore, recent complex clinical analyses, aimed at re-evaluating family histories of cases of Parkinson's disease, showed a significantly higher incidence of parkinsonian symptoms among relatives. These findings suggest autosomal dominant inheritance of the disease.[2] Under these circumstances, several genes have been proposed as candidate genes for Parkinson's disease.[3] However, the association of these candidate genes with the disease is still controversial.

Several large, multigeneration families with parkinsonism have been described. Among them, the Italian autosomal dominantly inherited pedigree reported by Golbe *et al*[4] and Polymeropoulos *et al*[5] has received attention because clinical features are similar to those of sporadic Parkinson's disease. Although the mean age at onset of the illness is somewhat earlier, each affected person in this pedigree closely resembles a case with idiopathic Parkinson's disease in clinical symptoms and therapeutic effectiveness of levodopa. Moreover, as in idiopathic Parkinson's disease, there are some variations in initial symptoms among the affected members of the family. For example, some presented with rest tremor, bradykinesia, and rigidity, whereas others presented with an akinetic rigid symptom, but without tremor. In addition, postmortem examination showed pathological changes with Lewy bodies, mimicking those of idiopathic Parkinson's disease. In this pedigree, it has been recently reported that genetic markers on chromosome 4q21-q23 (D4S2380 and D4S1647) are linked to the parkinsonism.[5] Here, we investigated a possible relation of the genetic marker D4S1647 to Japanese idiopathic Parkinson's disease by allelic association study.

We studied 111 patients with sporadic Parkinson's disease (age 64.6 (SD 9.7) range 35–81), diagnosed by a combination of three of the following neurological features: tremor, rigidity, bradykinesia, and postural instability. Levodopa therapy was effective in all patients. Cases of secondary parkinsonism due to other neurological diseases, chemicals, or toxins were excluded. One hundred and two patients (age 69.0 (SD 10.1); range 47–95) with old cerebrovascular disease were chosen as age matched controls, because we could strictly exclude Parkinson's disease in these cases. All subjects were Japanese. Genomic DNAs were extracted from leucocytes by conventional procedures. The region containing the genetic marker D4S1647, consisting of ATAG tetranucleotide repeats on chromosome 4q21-q23, was amplified by polymerase chain reaction (PCR). The PCR assays were performed with 27 cycles of denaturation at 94°C for 30 seconds, annealing at 55°C for 75 seconds, and extension at 72°C for 15 seconds, followed by a final extension at 72°C for six minutes. A fluorescence labelled primer p1(5'-TATTTCCAACACCCCTGCTA-3') and an unlabelled antisense primer p2 (5'-AAGCAAAGAGGATTGAAAGTG-3') were designed according to the Genome Data Base (http://gdbwww.gdb.org) and the Cooperative Human Linkage Consortium database (http://www.chlc.org). The PCR products were analysed with a laser based automated DNA sequencer (Pharmacia). Allele frequencies were statistically compared between Parkinson's disease and controls using Bonferroni's method.

Frequency of the polymorphism for a (ATAG)n repeat in D4S1647

	Control (n=102)	*PD (n=111)*
Age (mean (SD))	69.0 (10.1)	64.6 (9.7)
Allele repeats:		
9	0.485	0.505
10	0.010	0.023
11	0.039	0.036
12	0.177	0.207
13	0.211	0.153
14	0.074	0.077
15	0.005	0.000

The table shows the allele frequencies of each group. The (ATAG)9 allele is the most common in the Japanese population. There were no significant differences in allele frequencies between patients with Parkinson's disease and controls. Another common neurodegenerative disease, Alzheimer's disease, also consists of inherited and non-inherited cases. The existence of several familial Alzheimer's disease pedigrees prompted us to elucidate several genes responsible for the pathogenesis. Clinical and pathological features of these patients with familial Alzheimer's disease are similar to those of patients with sporadic disease, and recent data on the responsible genes have greatly contributed to our comprehensive understanding of the common neurodegenerative processes, which may occur in both familial and sporadic Alzheimer's disease. The ApoE ε4 allele has been shown to be associated not only with late onset familial Alzheimer's disease but also with sporadic disease.[6] The Parkinson's disease phenotype, linked to chromosome 4q21-q23, showed a high degree of penetrance and therefore it is not plausible that the same mutation is also responsible for idiopathic Parkinson's disease. However, other possible mutations in the same responsible gene may associate with milder clinical manifestations and a low degree of penetrance, mimicking idiopathic Parkinson's disease. Although this microsatellite is not a very informative marker because of low genetic variation and our results could not show a direct relation between familial and idiopathic Parkinson's disease, the discovery of this novel candidate locus opens up a new avenue for elucidating a putative common pathway responsible for "Lewy body type" neurodegeneration.

Addendum

Polymeropoulos et al recently identified a mutation in the α-synuclein gene in this locus (Science 1997;276:2045–7).