people homozygous for allele 122 (12 CA repeats, named allele 2 by Pravica *et al*[5] and allele 6 by Awata *et al*[6]) than in those of other genotypes.[5] Therefore, we investigated the CA repeat polymorphism of the IFN-γ gene in 170 patients with idiopathic Parkinson's disease (102 women and 68 men, aged 64.2 (SD 9.7) years; onset, 55.5 (SD 10.6) years; disease duration 8.7 (SD 5.2) years). As controls, 157 healthy people were selected from the annual health examination at a city clinic. The control group was matched for age (mean: 62.5 (SD 8.7) years), sex ratio (98 women and 59 men), and birth place (Kyoto and Osaka prefectures) with the patients. All participants were Japanese. The study protocol was approved by the institutional ethics committees and informed consent was obtained from every participant. The CA repeat polymorphism was analyzed according to a previous report.[6] The result is shown in table 1. Using χ^2 analysis (combined rare alleles "116", "118", "130", and "132"), no significant difference was found in allele distribution between the Parkinson's disease and control groups (p=0.86). When patients were divided into two groups (early onset and late onset disease), pc was obtained by multiplying the p value by two. No significant difference was found between patients with early onset Parkinson's disease and controls (pc=0.23) or between those with late onset Parkinson's disease and controls (pc=1.17). However, the allele distribution was significantly different between early onset (<50 years) and late onset (≥50 years) disease (χ^2=14.3, df=5, pc=0.028). The frequency of allele 122 was lower in those with early onset Parkinson's disease than in those with late onset Parkinson's disease. Carriership analysis also showed a low allele 122 carrier frequency in patients with early onset compared with late onset disease (χ^2=4.62, df=1, pc=0.039). Although the genetic polymorphism of IFN-γ does not seem to be a risk factor for Parkinson's disease, a lack of high producer allele 122 may affect the onset of disease. The allele 122 may be part of a haplotype that also includes functionally relevant polymorphisms. Our findings support the idea that the increase of IFN-γ concentration in the brain of patients with Parkinson's disease might be a compensatory response rather than a trigger of the disease. Thus, IFN-γ might be helpful in delaying the progress of the disease.

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Autonomic dysreflexia due to neurogenic bladder dysfunction; an unusual presentation of spinal cord sarcoidosis

Clinical involvement of the CNS in sarcoidosis is seen in about 5% of patients.[1] The most common affected sites are the basal leptomeninges and the region of the floor of the third ventricle. However, primary involvement of the spinal cord is much less common.[1] It may cause serious neurological deficits below the affected level of the lesion. Here we describe a case of spinal cord sarcoidosis with an unusual presentation: autonomic dysreflexia due to neurogenic bladder dysfunction.

A 42 year old woman began to have a slowly progressive spastic gait, left hand numbness, urinary urgency/frequency, and voiding difficulty which worsened gradually for a year. She underwent C2–7 laminoplasty for a relief of C4–6 cervical disc herniation where mild cord swelling was present. However, her gait difficulty ameliorated only for 2 weeks. Two months later she became unable to walk without an aid. Spinal MRI disclosed C2–7 cord swelling. She also developed bilateral hilar lymphadenopathy, ocular uveitis, and an increased serum concentration of angiotensin converting enzyme (ACE). Endoscopic lymph node biopsy showed non-caseating epithelioid granuloma. These findings and the clinical features confirmed the diagnosis of spinal cord sarcoidosis. She underwent steroid pulse therapy (1000 mg/day of intravenous methylprednisolone over 3 succeeding days) and started taking oral prednisolone (60 mg/day) with benefit. Steroids were tapered to 40 mg every other day and 4 months later she was referred to our hospital. However, her gait difficulty relapsed together with urinary urge incontinence and voiding difficulty. She had constipation but no orthostatic hypotension. On admission to our hospital, she had spastic tetraparesis, which was dominant in the legs. Deep tendon reflexes were brisk with positive Babinski's signs. Sensations for pin prick and proprioception were decreased bilaterally below the C6 dermatome. Routine laboratory data were normal. Examination of CSF showed normal cell count (lymphocyte 1/mm^3) but mildly increased protein content (42 mg/dl). The ACE concentration was normal both in the serum and CSF. Spinal MRI disclosed C2–7 cord swelling which appeared as low signal intensity on T1 weighted images and high signal intensity on T2 weighted images (fig 1). Gadolinium-DTPA images showed contrast enhancement in the C4/5 intramedullary region which extended longitudinally through the surface of the spinal cord. She again underwent three courses of steroid pulse therapy and started taking oral prednisolone (40 mg/day) and cyclosporin (200 mg/day), which gradually ameliorated her neurological symptoms.

However, she began to have a sudden onset of severe, throbbing headache twice a week, which was accompanied by conjunctival congestion, facial flushing, lacrimation, and congestion of the nose, without evidence of skeletal muscle spasms or bowel contraction. Just before the attacks she felt only slight bladder sensation. Measurement of the blood pressure showed an extreme hypertension (190/100 mm Hg) without increasing heart rate (60 beats/min), although it showed a normal value between these attacks. On the first attack emergent brain CT disclosed no subarachnoid hemorrhage and 5 mg of sublingual nifedipine was applied. Autonomic dysreflexia was suspected and the bladder was catheterised, which showed a urine volume of 650 ml. These treatments ameliorated all of her symptoms and the hypertension within 30 minutes. We performed urodynamic studies, which showed voluntary voided volume of 79 ml with low maximum and average flow rates.[2] She had a postvoid residual volume of 350 ml (normal<30 ml). On EMG-cystometry, the first sensation was 350 ml (normal 100 ml−300 ml) and the maximum bladder capacity was

Table 1 IFN-γ allele and carriership frequencies in patients with Parkinson's disease (PD) and in healthy controls as well as in patient subgroups whose ages of onset are early (<50 y) and late (≥50 y)

	PD n (%)	Control n (%)	Early onset PD n (%)	Late onset PD n (%)
Allele (bp):				
116	1 (0.3)		1 (1)	
118	2 (0.6)	1 (0.3)		2 (0.8)
120	52 (15.3)	41 (13.1)	23 (23)	29 (12.1)
122	157 (46.2)	143 (45.5)	35 (35)	122 (50.8)
124	19 (5.6)	16 (5.1)	8 (8)	11 (4.6)
126	93 (27.4)	92 (29.3)	28 (28)	65 (27.1)
128	9 (2.6)	8 (2.5)	1 (1)	8 (3.3)
130	1 (0.3)	1 (0.3)	1 (1)	
132	6 (1.8)	12 (3.8)	3 (3)	3 (1.3)
Total	340	314	100	240
Carriership:				
122 carrier	117 (68.8)	109 (69.4)	28 (56)	89 (74.2)
122 non-carrier	53 (31.2)	48 (30.6)	22 (44)	31 (25.8)
Total	170	157	50	120

For combined alleles 116, 118, 130, and 132, allele frequency: early onset PD *v* late onset PD χ^2=14.3, df=5, Pc=0.028.
Carriership frequency: early onset PD *v* late onset PD χ^2=4.62, df=1, Pc=0.039.

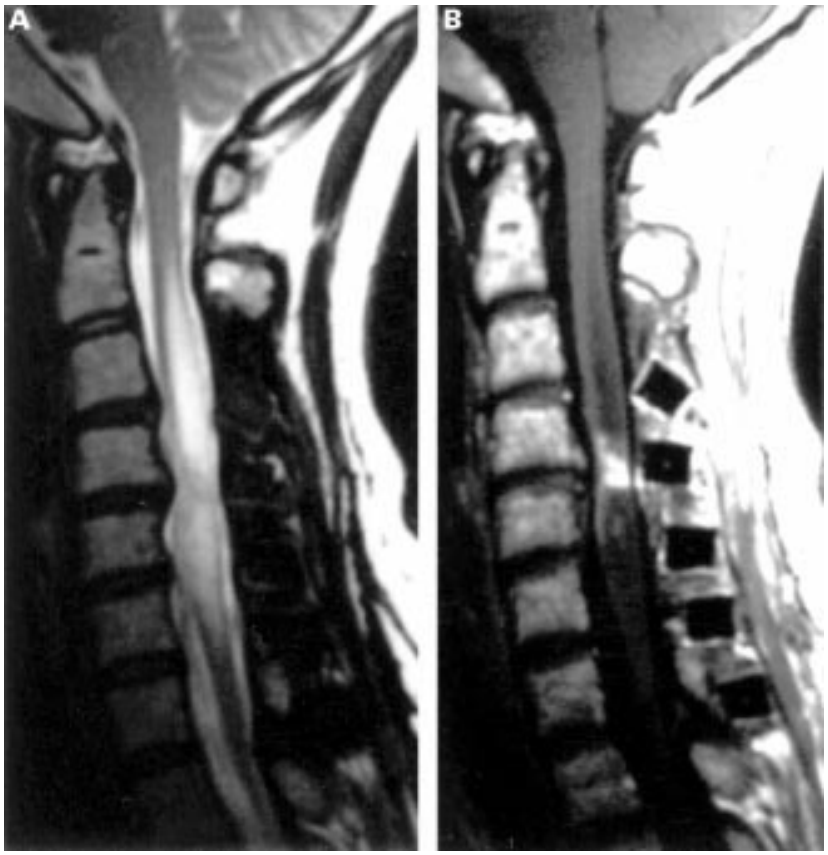

Figure 1 MRI of the spinal cord (sagittal plane). (A) T2 weighted images, (B) T1 weighted images with gadolinium enhancement). MRI disclosed C2–7 cord swelling. The intramedullary region of the swelling cord was low on T1 weighted images and high signal intensity on T2 weighted images. Gadolinium-DTPA images showed contrast enhancement in the C4/5 intramedullary region which extended longitudinally through the surface of the spinal cord.

670 ml (normal 200 ml−600 ml), indicative of impaired bladder sensation. A detrusor hyperreflexia was noted at the end of bladder filling. When asked to void after the detrusor hyperreflexia, her detrusor pressure increased slightly with poor urinary flow although the rectal catheter was pulled off at the end of voiding. There was no detrusor-sphincter dyssynergia. In the pressure-flow analysis[2] the point of a detrusor pressure (Pdet) at a maximum urinary flow rate (Qmax)—that is, PdetQmax—indicated equivocal obstruction (Abrams-Griffiths' nomogram) and normal detrusor contraction (Schäfer's nomogram). Above results indicated the presence of neurogenic bladder dysfunction. To avoid bladder distension, she was taught clean intermittent self catheterisation and started taking 2 mg/day oral prazosin hydrochloride, a selective α1-antagonist. After starting these treatments, her autonomic dysreflexia successfully ameliorated together with voiding difficulty, and her residual urine volume was lessened to 100 ml.

Autonomic dysreflexia is a syndrome of paroxysmal hypertension, headache, sweating, vasodilatation, and bradycardia. This syndrome consists of sympathetic discharge below the level of the cord lesion in response to afferent stimuli that would be innocuous in the normal person. Reflexive parasympathetic discharge occurs above the level of the lesion. It affects 66%–90% of all patients with complete spinal cord injury at the T5 dermatome or above.[3 4] It may occur among patients with incomplete spinal cord injuries, although the reaction seems to be milder than in those with complete lesions. Causes of spinal cord lesions other than traumatic have also been reported to give rise to autonomic dysreflexia,—for example, intramedullary haemorrhage caused by a spinal haemangioma or a spinal astrocytoma mimicking a pheochromocytoma. This is the first report showing a spinal cord sarcoidosis to be a cause of autonomic dysreflexia. As in the patients with spinal cord injury,[3 4] attacks of autonomic dysreflexia in our patient were most commonly precipitated by neurogenic bladder dysfunction, although it occurred with only slight bladder sensation. Urodynamic studies showed the presence of detrusor hyperreflexia. Detrusor hyperreflexia may reflect lesions in the lateral columns of the spinal cord,[5] which contain centrifugal pathways from the pontine micturition centre to the sacral preganglionic cells innervating the detrusor. Urodynamic studies also showed voiding difficulty with large postmicturition residuals without presence of detrusor-sphincter dyssynergia, although we did not assess bladder neck function in the patient. Studies of autonomic dysreflexia in patients with spinal cord injury showed that the rise in blood pressure is closely associated with not only the voiding phase but also the urinary filling phase, in which detrusor hyperreflexia and bladder distension are the common features.[3] Furthermore, our patient had impaired bladder sensation, most probably reflecting lesions in the dorsal column of the spinal cord.[5] Impaired bladder sensation may allow the bladder to distend silently, easily leading to autonomic dysreflexia. The patient was taught clean intermittent self catheterisation and started taking oral prazosin hydrochloride, a selective α1-antagonist, with benefit. During autonomic dysreflexia, concentrations of plasma noradrenaline (norepinephrine) increase and other substances—such as neuropeptide Y—may also increase in certain regions.[4] The bladder neck (internal urethral sphincter) is innervated by sympathetic nerve and abundant with α1A/D-adrenergic receptors. The α1-antagonists relax both vascular (mainly α1B) and urethral (mainly α1A/D) smooth muscles, which may account for the amelioration of both autonomic dysreflexia and neurogenic bladder dysfunction in the patient.

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The late whiplash syndrome: a biopsychosocial approach

In their admirable review, Ferrari and Schrader[1] re-introduce[2] the biopsychosocial model which recognises that the late whiplash syndrome is not the result of a chronic injury. They note the influence of compensation incentives such as that seen in Switzerland and other western countries. It is the high percentage of patients with chronic pain attributed to accidents that provide the greatest health care and economic burden,

The biopsychosocial model considers an effect of cultural expectation, cultural factors that generate symptom amplification and attribution. I agree with their conclusion that it negates the concept of "chronic injury",[3] but at the same time takes away the stigmata of the psychiatric label, while explaining that people's behaviour in response to their injury may generate much of the illness. The authors surprisingly neglect the final mechanism of the symptoms so often claimed in medicolegal practice, but so seldom encountered in the hospital clinic. They seem to blame cultural expectations and society at large, but they fail to consider the "victim",