Letters

Cigarette smoking, Parkinson's disease and ulcerative colitis

Sir: Individuals who develop Parkinson's disease are about twice as likely to have been habitual non-smokers when compared with a control population.1–4 Smoking also seems to exert considerable protective effects against ulcerative colitis.4–6 It has been suggested that both these illnesses may be associated with inflexible, morose, inward-looking personalities.7 8 One of us was struck by what was possibly an unrecognised association between these two conditions, five patients with both illnesses coming to light over a three year period. With the help of a letter expressing interest in this link which was published in the UK Parkinson's Disease Society Newsletter and further postal questionnaires and correspondence with the patients' general practitioners, 20 more people with both diseases were found. The mean age of all 25 patients (14 men, 11 women) was 62 years (range 43–79); six were in social class 1, eight in social class 2, six in social class 3, four in social class 4 and one in social class 5. In 19 the ulcerative colitis preceded the Parkinson's disease, sometimes by many years. Twenty of the patients had never smoked tobacco, three had given up 25, 21 and 10 years ago respectively; one was a very occasional pipe smoker and the other patient had smoked ten cigarettes a day all his life.

The prevalence of non-smoking for an age-sex-social class matched population in the United Kingdom would be about 50%.9 Two of the ex-smokers in the study had stopped smoking at least ten years before the onset of their Parkinson's disease or ulcerative colitis; another smoked a pipe very occasionally. Eighty per cent of the patients had never smoked tobacco and only three (12%) were smoking tobacco at all at the time of onset of one or other disease. In these the quantity smoked was fairly small (15 cigarettes/day, 10 cigarettes/day and 1/2 oz (14 g) tobacco/week). Although derived from a highly selected cohort, these figures would be in keeping with the reported negative association between smoking and both ulcerative colitis and Parkinson's disease.

Further prospective epidemiological studies should examine the possible link between these two diseases further and in particular the tantalising notion of a shared distinctive pre-morbid personality.

K BIHARI
AJ LEES

References


8 Todes CJ, Lees AJ. The pre-marked personality of patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 1985;48:97–100.


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HLA-DR2 negative narcolepsy

Sir: Association between narcolepsy and HLA-DR2 antigen is the strongest so far described between an HLA antigen and a disease.1–3 Among 28 narcoleptic patients, we found two HLA-DR2 negative cases. We present their case-reports and discuss the implications of these data.

We consulted the files of the patients suffering from narcolepsy and referred to the Hôpital Neurologique, Lyon since its inauguration in 1965. We found 28 patients. Short REM sleep latency was recorded by 24-hour polysomnography at least once in 24 patients. The other four patients had typical narcolepsy-cataplexy attacks. 50 HLA-A, B and C, 12 HLA-DR and 2 HLA-DQ highly serologically defined antigens were studied in every patient as previously described.4,5 Typing for HLA-DW2 and its subsets was also performed as reported.5 Results were compared with a control population of Caucasian blood donors. Chi-square test was used with a correction of probability values according to the number of HLA antigens studied. The level of significance was chosen at p < 0.05.

Increases in the proportions of cases with HLA-DQW1 (100%), DR2 (92–99%), DW2 (92–99%) and B7 (50%) antigens were the only significant observed differences when narcoleptic patients were compared with controls (table). The 26 DR2 positive narcoleptic patients were all DR2 long/DQW1/DW2.

Two patients were DR2/DW2 negative. The first one was a Caucasian 54 year old female phone operator with A2 A30/82, BW62/CW3/DRW13 DRW14/DQW1 antigens. Typical sleep attacks began at age 46 years, up to 5 times per day. They were controlled initially with 75 mg desipramine. Treatment with clomipramine was stopped owing to dizziness and was replaced by 100 mg clomipramine with good efficacy and tolerance. Excessive daytime somnolence was another salient feature. Nocturnal sleep was self-estimated as excellent and, usually, 10 hours long. However, there was a transient fatigue on awakening. No actual cataplexy attacks, sleep paralysis and hypnagogic hallucinations were experienced. A 24-hour polygraphic recording was made in February 1986 after a 2 weeks cessation of drugs. It showed four sleep episodes with direct REM sleep. Total sleep duration was 12 h 30 min with a relative excess of REM sleep (43%). Otherwise, since puberty, there were typical symptoms and signs of dystrophy myotonica (Steinert's disease) with myotonic discharges in the EMG. At the last examination in August 1986, our patient was still minimally affected by the muscle disorder in her daily activity. She had no respiratory insufficiency. A brother had both narcolepsy and Steinert's disease. He died from myocardial infarction at age 44. Two sisters were operated on for bilateral cataracts in their fourth decade. A brother and a sister were unaffected. We were aware of one case of muscle disorder, one case of early cataracts and one case of early baldness in the paternal lineage.

K BIHARI
AJ LEES

Department of Neurology, Middlesex Hospital, Mortimer Street, London W1N 8AA, UK

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Sir: Association between narcolepsy and HLA-DR2 antigen is the strongest so far described between an HLA antigen and a disease.1–3 Among 28 narcoleptic patients, we found two HLA-DR2 negative cases. We present their case-reports and discuss the implications of these data.

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The second DR2 negative narcoleptic patient was a 35 year old lorry driver of Reunion Island origin. He was born and lived there until his moving to Lyon at age 29. Cataplexy attacks occurred 2 years later, soon followed by sleep episodes and severe nocturnal dysnomia. Polysomnography showed short REM sleep latency. The patient was unaware of a similar case in his family. He was HLA A36 A26/B7 B35/CW4/DRW1 DRW13/DQW1 DQW3. The presence of the A36 antigen indicated his negroid ancestry which was otherwise visible.

In this study, we were able to confirm the extraordinary association between narcolepsy and HLA-DR2 antigen. However, two patients were DR2 negative. One of them was negroid. The other patient was remarkable as narcolepsy was combined with dystrophia myotonica, an exceptional association.6 7

These data have several implications. Firstly, they confirm that narcoleptic patients, especially negroids, may be HLA DR2 negative.8 9 10 It follows that the absence of the HLA-DR2 antigen is not sufficient to reject the diagnosis. Above all, the gene coding for DR2 antigen is not per se responsible for narcolepsy. All of our patients were HLA-DQW1 positive, as were the 156 patients DQ typed in the literature.11 12 13 14 Studies on the correlations between HLA class II specificities and DNA Restriction Fragments Length Polymorphism (RFLP) defined with HLA-DQβ cDNA probes have shown that DQW1 can be divided in at least three types,14 the same being present in all narcoleptic patients.13 14 The gene coding for DQW1 may be the primary association with narcolepsy and the causal factor for the disease. Another possibility is that it is simply closer to the hypothetical narcolepsy susceptibility gene than the gene coding for DR2. Further work, using RFLP studies with new restriction enzymes or DNA sequencing, is necessary to test these hypotheses and to localise precisely the susceptibility gene. Two more questions need elucidation: why the narcolepsy susceptibility gene is in such a tight linkage disequilibrium with the DR2 and DQW1 alleles? What are the mechanisms linking the gene to the disease?

CHRISTIAN CONFAVEUX,*
LUCETTE GEBUHRER,†
HERVÉ BETUEL,†
CATHERINE FREIDEL,†
HELÈNE BASTUJI,†
GILBERT AIMARD,†
MICHEL DEVIC,†
MICHEL JOUVENT,†
Hôpital Neurologique, and Centre de Transfusion Sanguine, Laboratoire d’histocompatibilité,† Lyon, France

Correspondence to C Confaveux, Hôpital Neurologique, 59 boulevard Pinel, 69003, Lyon, France.

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References

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Letters

Pituitary apoplexy following isosorbide dinitrate administration

Sir: Pituitary apoplexy usually arises spontaneously in previously unsuspected pituitary adenomas. A variety of possible precipitating factors have been reviewed by Bernstein et al who described the first of three reported cases of pituitary apoplexy following a pituitary stimulation test.1 Apart from thyrotrophin-releasing hormone2 and bromocriptine3 no other vasoactive drugs have been implicated in the aetiology of this condition. We describe a patient who developed major apoplexy following oral isosorbide mononitrate.

A 54 year old man had an anterolateral myocardial infarction in August 1984 and was commenced on atenolol 100 mg daily. He underwent coronary angiography in March 1985 and was advised to commence isosorbide mononitrate (Elantan 20, Sanol Schiraz) 20 mg twice daily in addition to the atenolol. One to two hours after taking the first tablet he developed a severe vertical and left sided headache which lasted three hours and resulted in discontinuation of the isosorbide. One month later he attempted to restart the drug but 90 minutes after taking it