

LINK BETWEEN HLA-B40 AND DIALYSIS ENCEPHALOPATHY

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Summary

Not all patients with end-stage renal failure exposed to significant aluminium loading develop dialysis encephalopathy, suggesting that constitutional factors may play a part in the clinical expression of this disorder. We determined tissue types in 41 patients with dialysis encephalopathy diagnosed on strict criteria. The frequency of HLA-B40 was significantly higher in this group than in a healthy control population, implying involvement of genetic factors in the pathogenesis of dialysis encephalopathy.

Introduction

Aluminium poisoning is generally recognized as the cause of a syndrome of dialysis encephalopathy, fracturing osteomalacic osteodystrophy, and anaemia in patients on maintenance haemodialysis therapy [1]. The chief source of aluminium intake is the dialysis water supply [2], although oral aluminium-containing phosphate binders are the important secondary source [3]. Some patients never exposed to aluminium-rich dialysate develop the syndrome of aluminium intoxication whereas others do not become clinically aluminium-toxic despite years of dialysis against fluid containing very high concentrations of aluminium. Amongst cases of clinical aluminium intoxication, features of either dialysis encephalopathy or fracturing osteomalacic osteodystrophy may predominate. A possible explanation for these variations is that constitutional factors may affect the way in which aluminium is absorbed and metabolized. Such factors could be linked genetically with histocompatibility antigens. To test this hypothesis we compared the incidence of individual A and B locus antigens with their occurrence in a control population.

Methods

Clinical records of all patients on the maintenance haemodialysis programme in Cork and in Jervis Street since 1972 were reviewed. Diagnoses of dialysis

encephalopathy were established according to the criteria set out in Table I. Histocompatibility antigens for A and B loci were determined using standard microlymphocytotoxic techniques [4]. Frequencies of individual antigens were compared with their incidence amongst 453 healthy control subjects using the chi-square test with Yates' correction [5].

TABLE I. Dialysis encephalopathy: diagnostic criteria

I	On maintenance dialysis therapy for at least 18 months, or having undergone at least 150 haemodialysis sessions.
II	No other feasible explanation for neurological syndrome.
III	<i>Two or more of the following:</i> speech difficulty seizures myoclonus dyspraxia more than five pathological fractures, and/or positive aluminium staining of bone.
IV	<i>One feature from category III</i> <i>With three or more of the following:</i> change in mood change in behaviour episodic confusion related to dialysis intellectual deterioration asterixis serum aluminium greater than 50mcg/L diffuse EEG abnormality blood transfusions on 10 or more occasions over a 12 month period.

Results

The incidence of A and B locus tissue antigens was the same amongst the 41 cases of dialysis encephalopathy identified and in the control population with the exception of HLA-B40, which was significantly more frequent in the dialysis encephalopathy group (Table II; chi-square/Yates = 4.002; $p < 0.05$).

TABLE II. Fourfold Table for incidence of HLA-B40 in dialysis encephalopathy and control groups. Chi-square/Yates = 4.002. $p < 0.05$

	Negative	Positive	Total
Dialysis encephalopathy	33	8	41
Control	414	39	453
Total	447	47	494

Discussion

Many disorders have been found to have positive associations with specific tissue antigens, most notably the group of arthropathies associated with HLA-B27 [6]. Genes linked with those determining the histocompatibility antigens may predispose a subject to a disease that will develop once the appropriate environmental stimulus is encountered. Our finding suggests that such a mechanism may be involved in the pathogenesis of dialysis encephalopathy. The exact mode of this mechanism could relate to individual variations in gastrointestinal absorption of aluminium, distribution of an aluminium load within the body, or take-up of the element into tissues at a molecular level. Further work in this area may define more accurately groups of patients with constitutional susceptibilities to different aspects of aluminium intoxication and may help to identify individuals commencing maintenance dialysis therapy who require particular protection from aluminium exposure.

References

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