

Table 2 Physiological, haematological, and biochemical variables used in assessing prognosis in acute pancreatitis⁷

Systolic hypotension	<	90 mm Hg
Tachycardia	<	140
Fever	>	38.4°C
Prothrombin time	>	14 seconds
White cell count	>	20 × 10 ⁹ /l
Haematocrit	<	30%
Serum albumin	<	30 g/l
Serum creatinine	>	0.18 mmol/l
Serum urea	>	5 mmol/l
Serum bilirubin	>	69 mmol/l
Serum calcium	<	2 mmol/l

findings than the other indices studied, although Cassey's index is more likely to be completed. As has been stated above, indices requiring serial assays, or assays such as the PaO₂ in arterial blood which are not routinely carried out on admission, were less likely to permit a complete assessment of the patient's condition.

Although undiagnosed pancreatitis is

probably uncommon as a sole cause of death, the retrospective use of one or more of these indices may help assess the severity of the patient's condition on admission to hospital and in determining the contribution made towards a fatal outcome by the failure to diagnose and treat the acute pancreatitis.

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HLA antigens in Hungarian patients with idiopathic haemochromatosis

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Abstract

Thirteen unrelated patients with idiopathic haemochromatosis (eight men, five women) were studied. The diagnosis was based on clinical, biological, and histochemical findings. HLA typing was performed in all 13 and in all of their available first degree relatives (n = 31). HLA A3 was present in nine of 13 probands (69.2% compared with 18.8% in the group of 53 healthy blood donors and 22.4% in a selected Hungarian population (n = 1910). HLA B7 was present in five of 13 probands (38.4% compared with 11.3% and 14.6%). An A3B7 antigen association was found in five of 13 patients. The A3B7 haplotype was found in three, A2B12 and A2B38 haplotypes were found twice in 10 genotyped probands. Pedigree studies showed that there was one unaffected homozygote, 24 heterozygotes, and six non-carriers.

Extended family and population studies are necessary to establish the prevalence of the gene in Hungary and an association with haplotypes other than A3B7.

Idiopathic haemochromatosis is a recessively transmitted hereditary disease that is characterised by generalised parenchymal iron

overload, leading to liver cirrhosis, diabetes mellitus, cardiomyopathy, endocrine dysfunction, arthropathy and skin pigmentation.¹ The idiopathic haemochromatosis gene is closely linked to the HLA-A locus on chromosome 6²; A3, B7, and B14 are most strongly associated with it.³ The HLA marker for the idiopathic haemochromatosis allele is, in fact, haplotypic.³ In a family where one member has idiopathic haemochromatosis the HLA identical sibling should also be affected.⁴

We collected data on HLA distribution in patients with idiopathic haemochromatosis in Hungary so that we could assess the number of affected family members in a given population.

Methods

Thirteen unrelated patients (eight men and five women) aged 35 to 65 years were studied. Idiopathic haemochromatosis was diagnosed on clinical, biochemical, and histochemical grounds. HLA typing was performed in 13 probands and in all of their available first degree relatives (n = 31) through pedigree studies. Relatives sharing both, one, or no HLA haplotypes with the proband were regarded as either homozygous, heterozygous for the idiopathic haemochromatosis gene, or normal (non-carriers).⁴ Determinations of serum iron, iron binding capacity, and serum

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Table 1 Clinical, biochemical, and histological data of 13 unrelated Hungarian subjects with idiopathic haemochromatosis

Case No	Sex	Age † (years)	Clinical signs	Transferrin saturation (0.2–0.55)	Serum ferritin (20–200 ng/ml)	Liver biopsy	
						Iron grade	Histology
1. ■	M	52	Hepatomegaly, pigmentation, diabetes mellitus, arthropathy	0.90	3000	4 +	Cirrhosis
2. ■	F	42	Hepatomegaly	0.73	660	4 +	Cirrhosis
3.	M	39	Hepatomegaly, pigmentation, diabetes mellitus, cardiomyopathy, hypogonadism	0.93	1260	4 +	Cirrhosis
4.*	M	49	Hepatomegaly, pigmentation, arthropathy, hypogonadism	0.82	2000	4 +	Cirrhosis
5.*	M	39	Hepatomegaly	0.60	79	4 +	Normal
6.	F	60	Hepatomegaly, diabetes mellitus, arthropathy	0.78	3000	3 +	Fibrosis
7.	F	61	Hepatomegaly	0.65	640	3 +	Cirrhosis
8.	M	35	Hepatomegaly	0.74	1080	4 +	Normal
9.	F	47	Hepatomegaly	0.74	840	3 +	Normal
10.	M	41	Hepatomegaly	0.78	4280	4 +	Fibrosis
11. ■	M	60	Hepatomegaly, diabetes mellitus	0.76	500	4 +	Cirrhosis
12.	F	59	Hepatomegaly, pigmentation	0.88	660	3 +	Cirrhosis
13.*	M	59	Hepatomegaly, diabetes mellitus Clinically cirrhosis	0.86	225	No biopsy	

*Patients previously treated by phlebotomy.

† At the time of diagnosis.

■ The patient died after the study; the necropsy showed that he had had idiopathic haemochromatosis.

ferritin concentrations were carried out in all available family members and in 53 HLA typed blood donors who acted as controls. The HLA antigen distribution of the Hungarian population was determined by the HLA phenotype of healthy panel members, parents of patients waiting for organ transplantation, and couples involved in paternity testing, etc. The prevalence of HLA antigens in probands was compared with that of HLA antigens in the group of 53 healthy blood donors and in the Hungarian population (n = 1910).

Serum iron concentrations and total iron binding capacity were determined using standard techniques; serum ferritin concentration was measured by a radioimmunoassay. Sections of liver biopsy specimens were stained with Perls' Prussian blue for iron for histochemical evaluation. Hepatic siderosis was graded according to Scheuer from 0 to 4+.⁵ HLA typing was performed by the NIH lymphocyte cytotoxicity micromethod.⁶

Results

Table 1 shows the data on iron metabolism and the histological and clinical findings of each patient. In cases 1, 2, and 11 previous long term alcohol intake and exposure to insecticide sprays in case 12 were also aetiological factors in the formation of cirrhosis.

The prevalence of HLA antigens recorded in table 2 indicates that HLA A3 and B7 were more common in the patients with idiopathic haemochromatosis than in healthy blood donors or in the Hungarian population. HLA B14 was present in one patient. An association with HLA A3B7 was found in five of 13

patients. The genotypes of 10 of 13 unrelated probands and the phenotypes and genotypes of 31 first degree relatives were determined through pedigree studies. Twelve different haplotypes were found in 10 genotyped probands. The A3B7 haplotype was found three times, and A2B12 and A2B38 twice in seven of 10 probands. A3B7 was present in four of the seven children. Other haplotypes found once were: A1B8, A1B13, A1B38, A1B40, A2B15, A3B13, A3B27, A3B51, A3Bx, A11B7, A24B7, A24B12, and A32B12.

The pedigree analysis showed that there was one non-affected homozygote, who shared both proband's haplotypes. Transferrin saturation and serum ferritin concentrations were in the normal range (0.34 and 55 ng/ml, respectively); the sibling of case 10 had died one year previously of idiopathic haemochromatosis. Six family members were non-carriers, while 24 persons were heterozygotes. Transferrin saturation values were in the normal range in all non-carriers and in all but two of 24 heterozygotes. These two heterozygotes had transferrin saturation repeatedly above 0.70, but the serum ferritin concentration was normal.

Discussion

The HLA antigens A3, B7, and B14 are most strongly associated with idiopathic haemochromatosis.³ In all reported series the HLA antigen A3 had a higher prevalence in patients with idiopathic haemochromatosis than in control subjects, ranging from 55% to 100% in idiopathic haemochromatosis, compared with 19% to 32% in control populations.⁷ The HLA antigen B7 also had an increased prevalence (28–86%) in idiopathic haemochromatosis (v 9–34%) in controls; as for antigen B14, about half the studies reported an increased prevalence in idiopathic haemochromatosis compared with controls.⁷

Our results show that HLA A3 is also closely associated with idiopathic haemochromatosis in Hungary. HLA A3 was present in 69.2% of cases of idiopathic haemochromatosis compared with 18.8% and

Table 2 Prevalence of HLA antigens A3, B7, and B14 in patients with idiopathic haemochromatosis, healthy blood donors, and in a selected Hungarian population

	A3	B7	B14
Patients with IH (n = 13)	9 (69.2%)	5 (38.4%)	1
Healthy blood donors (n = 53)	10 (18.8%)	6 (11.3%)	2 (3.8%)
Hungarian population (n = 1910)	428 (22.4%)	279 (14.6%)	111 (5.8%)

22.4% in controls. The prevalence of HLA B7 was also higher in idiopathic haemochromatosis than in controls (38.4% v 11.3% and 14.6%).

An association between the haemochromatosis gene and the A3B7 haplotype has been seen in all series throughout the world.³ Associations with A3B14,^{3,8} A11B35 and A11B5,³ A1B8⁸ and A3B35⁹ were also observed in different countries.

The association with A3B7 was observed in five probands of our series. The A3 antigen showed linkage with other B, not B7, antigens in four probands. In five probands with A3B7 phenotype pedigree analysis showed that only four of five genotypes accorded with the proband's genotypes.

Our results agree with data reported from other countries; A3 is significantly more common on idiopathic haemochromatosis chromosomes regardless of the presence or absence of B7 or B14, and A3 (and to a lesser degree A11) is the independent idiopathic haemochromatosis allele marker.³

The number of heterozygotes, identified through pedigree studies, agrees with the expected prevalence according to published findings,¹⁰ the number of homozygotes, however, was small. The probability of finding HLA identical (homozygote) family members through pedigree studies is influenced by different factors: the recessive mode of inheritance, the gene prevalence in the population, and number of siblings in the family, etc.

The HLA identical, but disease free sibling,

was a 40 year old women with regular menses. The transferrin saturation value and the serum ferritin concentration were normal. She may be an example of incomplete expressivity or recombination.^{2,4} A detailed investigation of DNA polymorphism would be required to explain this finding. Extended family and population studies are necessary in Hungary to establish the prevalence of the gene and the likely role of haplotypes other than A3B7.

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Cytogenetic analysis of a granulocytic sarcoma in a patient without systemic leukaemia

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Abstract

Granulocytic sarcoma is a rare complication of leukaemia. Occasionally it presents before the development of systemic leukaemia when diagnosis may be difficult. A case of granulocytic sarcoma occurring in a patient with no overt evidence of leukaemia, but in whom cytogenetic analysis of the bone marrow showed a clonal t(12;13) translocation, is reported. Cytogenetic analysis of tissues in this disease may indicate evidence of systemic disease before overt morphological changes.

Granulocytic sarcoma is a rare tumour, defined as a "localised tumour mass composed of immature cells of the granulocytic series".¹ The most common sites of presentation are bone, periosteum, soft tissue, lymph node and

skin. The tumour may develop during the course of acute myeloblastic leukaemia (AML), chronic myeloid leukaemia (CML), or other myelodysplastic disorder. Alternatively, the tumour precedes leukaemia by some months.² When granulocytic sarcoma presents without blood or bone marrow manifestations of leukaemia, the diagnosis may be missed.³ Histological diagnosis can be difficult and many patients are initially diagnosed as having high grade lymphoma.⁴⁻⁶ Often the first indication of misdiagnosis is the lack of response to treatment.

Case report

A 52 year old man presented with a rapidly enlarging chest wall mass, initially thought to be a high grade non-Hodgkin's lymphoma. Staging investigations showed no evidence of disease elsewhere and he was treated with

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