tions, but these all return to normal within a week,¹⁻³⁰ whereas low density lipoprotein cholesterol concentrations rise again more slowly. Whether procedures designed to selectively remove low density lipoprotein but conserve high density lipoprotein and other proteins will prove to be as or more effective than plasma exchange remains to be shown.³¹⁻³³ Transplantation of the liver provides the most definitive approach to treatment currently available but necessitates long term immunosuppression, with its attendant drawbacks.³⁴⁻³⁵ We conclude that plasma exchange every two weeks offers a safe and proved means of improving prognosis in homozygous familial hypercholesterolaemia with which all newer forms of treatment can be compared.

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Emphysema, cirrhosis, and heart block in a young patient with partial α_1 antitrypsin deficiency (PiMZ phenotype)

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Abstract

Severe lung disease and liver disease are not recognised features of the PiMZ phenotype, which is associated with α_1 antitrypsin deficiency. A 31 year old woman with this phenotype was found to have emphysema and complete heart block and showed evidence

of hepatic cirrhosis, although her three sisters, all of whom had the same phenotype, were clinically normal.

This case supports the possibility of a causal relation between the PiMZ phenotype and chronic lung and liver disease, but an association between α_1 antitrypsin deficiency and complete heart block could not be proved in this patient.

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Introduction

It is not clear whether the α_1 antitrypsin PiMZ heterozygous state predisposes to lung disease.¹⁻⁴ We report on a patient with the PiMZ phenotype who at the age of 36 had severe emphysema, evidence of hepatic cirrhosis, and complete heart block. Neither severe lung disease nor liver disease is a recognised feature of the PiMZ phenotype, and heart block has not previously been reported in association with partial α_1 antitrypsin deficiency.

Case report

A 31 year old woman presented in 1980 with a three year history of respiratory symptoms. She had smoked 15 cigarettes a day for 12 years, denied alcohol intake, but had a history of neonatal jaundice. She had three clinically normal siblings, but her mother had chronic obstructive lung disease and was subsequently found to have α_1 antitrypsin deficiency (see table). The patient's chest was hyperinflated, the forced expiratory volume

phatase 207 U/l (normal range 30-140 U/l), and γ -glutamyltransferase 165 U/l (normal range 6-31 U/l). Bilirubin and albumin concentrations and aspartate transaminase and alanine transaminase activities were normal. Previously all biochemical tests, including liver function tests, had yielded normal results. Technetium isotope scanning confirmed the diagnosis of hepatomegaly and showed multiple areas of focal replacement consistent with cirrhosis. Tests for hepatitis B surface antigen and antismooth muscle and antimitochondrial antibodies gave negative results, and serum con-

α_1 Antitrypsin concentrations and activities in relation to phenotypes of patient and her family

	Date of birth	Phenotype	α_1 Antitrypsin concentration (g/l) (% of mean normal concentration)	α_1 Antitryptic activity as % of mean normal activity
Patient	15 Feb 1949	PiMZ	1.8 (75)	88
Mother	21 Apr 1913	PiZZ	0.4 (17)	17
Sister	19 Oct 1947	PiMZ	1.4 (58)	47
Sister	7 May 1950	PiMZ	1.5 (63)	65
Sister	28 Mar 1955	PiMZ	1.4 (58)	60

in one second being 1.1 litres and the vital capacity 2.3 litres, with no improvement when she used a bronchodilator. Lung volumes showed hyperinflation, with a residual volume of 3.6 litres (predicted 1.5 litres) and a ratio of residual volume to total lung capacity of 73%. Carbon monoxide transfer factor was 3.24 mmol/min/kPa (9.7 ml/min/mm Hg) (53% of the predicted normal value). A radiograph of the chest (figure) showed hyperinflation with flattening of both hemidiaphragms and a peripheral vascular pattern suggestive of emphysema. Computed tomography con-

centrations of iron, transferrin, ferritin, and α fetoprotein were all within the normal reference ranges. Results of liver function tests and isotope scanning remained abnormal. In December 1983 she developed a recurrent left pneumothorax, which was treated with kaolin pleurodesis. Liver biopsy was not performed because of the possible risk of right pneumothorax.

Comment

The PiMZ phenotype occurs in 3-4% of the British population and is associated with an α_1 antitrypsin serum activity roughly 60% of the normal value.¹ Studies to assess the risk of lung disease in subjects with this phenotype have differed in their conclusions. Subjects with the PiMZ phenotype who smoke have been reported to be more likely to develop clinically important lung disease than those with the phenotype who do not smoke and those with the PiMM phenotype who do.² It has also been concluded, however, that subjects with the PiMZ phenotype do not have a predisposition for developing severe pulmonary disease.³ A necropsy study suggested that the PiMZ phenotype predisposes to both liver and lung disease.⁴

Our patient was most unusual in that she developed emphysema before the age of 31. She also had evidence of hepatic cirrhosis, for which no aetiological reason was found. Although there is a clearly established association between homozygous Z deficiency and cirrhosis, the risk in subjects with the PiMZ phenotype is less clear.^{4, 5}

This report supports the argument that the PiMZ phenotype is causally related to severe chronic lung and liver disease. We must, however, concede that this patient's three sisters, all of whom had the PiMZ phenotype and appropriately reduced concentrations and activities of α_1 antitrypsin (table), had normal chest radiographs, lung volumes, transfer factors, liver function, and resting heart rates. A relation between complete heart block and α_1 antitrypsin deficiency has not been described before, and such an association in this patient can be only conjectural.

Radiograph of chest showing hyperinflation.

firmed the presence of bilateral basal bullae. The table gives details of the α_1 antitrypsin states of the patient and her family. Phenotyping was performed by thin layer agarose isoelectrofocusing with imprint immunofixation. Serum concentrations were estimated by immunoturbidimetry using a centrifugal analyser standardised to give a value of 2.4 g/l for pooled normal adult serum. Serum antitryptic activities were determined enzymatically.

During 1981 she suffered blackouts and was found to have complete heart block. A permanent transvenous pacemaker was inserted and the blackouts did not recur.

In January 1983 she was found to have hepatomegaly and deranged results of liver function tests but no evidence of right ventricular failure (lactate dehydrogenase activity 550 U/l (normal range 72-395 U/l), alkaline phos-

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