Modification of the \( \alpha_1 \)-antitrypsin phenotype in neonatal hepatitis

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SUMMARY Two cases of neonatal hepatitis are described, one related to cytomegalovirus infection and the other idiopathic. In both infants a transient abnormality of the \( \alpha_1 \)-antitrypsin phenotype, inconsistent with the parent's phenotypes, reverted to normal during the convalescent phase of the illness.

Case 1
A girl of 36 weeks' gestation, who weighed only 1015 g at birth, developed a conjugated hyperbili-rubinaemia from her eighth day of life. Her mother had a non-specific viral illness with a rash at about 24 to 26 weeks' gestation.

Investigation showed evidence of cytomegalovirus infection in urine culture and throat swab. Both mother and child had a cytomegalovirus titre of 40 by complement fixation. Other virology and toxoplasma titres were negative. In addition she had an \( \alpha_1 \)-antitrypsin titre of 1.7 g/l (normal range 1.8 to 3.0 g/l) with a P,M phenotype, despite both parents being P,M. She reverted to a P,M phenotype by the age of 11 months.

Her developmental progress has been mildly delayed with bilateral hearing impairment and poor growth. There is no evidence of persisting hepatic pathology at the age of 2 years.

Case 2
A boy of 33 weeks' gestation, who weighed only 780 g at birth, developed a conjugated hyperbili-rubinaemia from his eighth day of life. His mother had sickle cell disease and had required the transfusion of 19 U of blood during pregnancy. She had had transient jaundice with severe itching at 26 weeks' gestation.

Investigation showed a normal hepatic ultrasound, negative virology and toxoplasma titres, and negative urine culture for cytomegalovirus. The urine showed no notable increase in reducing substances. His \( \alpha_1 \)-antitrypsin value was 1.3 g/l (normal range 1.8 to 3.0 g/l) with a P,M phenotype. His parents' phenotypes were P,M. During the convalescent phase, at the age of 10 months, when his liver function tests had returned to normal, his phenotype reverted to P,M with an \( \alpha_1 \)-antitrypsin value of 1.9 g/l.

He has persisting poor growth, but his development seems to be progressing satisfactorily.

\( \alpha_1 \)-antitrypsin phenotyping was performed in both cases by isoelectric focussing on an acrylamide gel.

Discussion
\( \alpha_1 \)-antitrypsin is a protease inhibitor. Deficiency of this protein may be associated with neonatal hepatitis in addition to hepatic cirrhosis\(^1\),\(^2\) and pulmonary emphysema.\(^3\)

Phenotypic alleles of \( \alpha_1 \)-antitrypsin are classified by Latin letters on the basis of their electrophoretic mobility on starch gel electrophoresis. P,M is the phenotype associated with normal \( \alpha_1 \)-antitrypsin values. Subjects with P,ZZ phenotype have only 15% of normal activity, and are more prone to...
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I thank Dr K L Dodd, Consultant Paediatrician, Derby City Hospital for permission to discuss two of his patients and Dr A Milford-Ward, Director, Supraregional Protein Reference Unit, Sheffield for his helpful advice.

References

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Received 20 November 1984

Oxandrolone in low dose for constitutional delay of growth and puberty in boys

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SUMMARY Twenty four boys with delayed pubertal growth spurt were treated with oxandrolone (2.5 mg daily) for 0-21 to 0-65 years. The mean increment of growth velocity was 4.4 cm/year during treatment, which was maintained at 3.7 cm/year after treatment. There was no significant change in height for bone age standard deviation scores.

Constitutional delay of growth occurs in otherwise healthy adolescents with stature reduced for chronological age but generally appropriate for bone age and the stage of pubertal development, both of which are usually delayed. There is often considerable delay in the onset of the puberty growth spurt which may cause severe psychological disturbance. Oxandrolone (17$^{\beta}$-hydroxy-17-methyl-2-oxa-5$^{\alpha}$-androstan-3-one) is one of a group of anabolic steroids derived from testosterone which accelerate growth.

Patients and methods

Twenty four, short, pubertal boys (testicular volumes more than 3 ml) were treated with oxandrolone because of severe psychological disturbance. Two had mild asthma and one had severe psoriasis which had been treated with topical fluorinated corticosteroids. The heights of all patients were less than the 3rd centile for chronological age, except for one, whose height was on the 10th centile. Fourteen had delayed puberty with testicular volumes less than the 10th centile for chronological age. Mean bone

hypothalamic-pituitary axis, and hepatotoxicity but the most serious problem is the potential to advance bone age disproportionately to height gain, which compromises final adult height. The poor reputation that anabolic steroids have gained may partly be due to the large doses which were first used.

1 Growth acceleration does not seem to be related to dose but advance in skeletal maturation is. We have attempted to define an effective treatment regimen, free of side effects, using oxandrolone.

The Z band is observed to migrate cathodally to the M band.

In these two patients there was an abnormal protein migrating similar to that of the Z band during the acute phase of the hepatitis. This was incompatible with the parents' phenotypes and resolved during the recovery phase. This phenomenon has been seen once previously in neonatal hepatitis associated with cytomegalovirus infection. It may be caused by 'switching on' of the production of an abnormal protein during the acute phase of the illness, or to decreased post ribosomal sialylation of the normal M protein. This has yet to be clarified.

It is important to be aware of this transient abnormality, which may occur in neonatal hepatitis, and to check both parents' $\alpha_1$-antitrypsin phenotypes. This may avoid erroneous counselling in respect of the prognosis and the genetic implications.

develop subsequent pulmonary and hepatic complications. Phenotype P,MZ will produce intermediate values of $\alpha_1$-antitrypsin (approximately 50%) which may be associated with liver disease. 4 The Z band is observed to migrate cathodally to the M band.

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Arch Dis Child 1985 60: 378-379
doi: 10.1136/adc.60.4.378

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