

PostScript

LETTERS

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Another case of HBV associated membranous glomerulonephritis resolving on lamivudine

Connor and colleagues¹ (see page 446) report rapid resolution of a hepatitis B associated membranous glomerulopathy and nephrotic syndrome after two months of oral lamivudine. We would like to add our experience with lamivudine in a similar case.

A 5 year old female of Vietnamese origin presented with a two week history of periorbital swelling and weight gain. She had 3 plus protein, 10-20 dysmorphic red blood cells, and red blood cell casts in her urine. Serum albumin was low at 19 g/L, cholesterol was 9.8 mmol/L, and serum complement C3 and C4 were reduced (0.61 g/L and <0.1 g/L, respectively). She was hepatitis B surface antigen positive and hepatitis B surface antibody negative. The physician caring for her at that time placed her on prednisone 60 mg/m²/day in three divided doses, and referred her to our service six weeks later, as the nephrotic syndrome was unresponsive to steroids. Her viral load initially was 1090 pg/ml of hepatitis B DNA in peripheral blood, and rose to >2000 pg/ml after four weeks of steroids, when ALT peaked at 72 U/L. A renal biopsy revealed stage II membranous glomerulonephritis. A liver biopsy showed focal lobular and portal inflammation and changes consistent with a mild chronic hepatitis.

She was started on lamivudine at a dose of 50 mg once daily (2.5 mg/kg), with steroids being weaned off over four weeks. Two weeks later the hepatitis B DNA dropped to 1686 pg/ml, decreased to 7 pg/ml two months later, and was undetectable at three months. She continued to be hepatitis e antigen positive without detectable e antibodies. The patient's proteinuria was cleared after three months of treatment, and serum albumin remained normal thereafter. She continued to take lamivudine for 13 months without rebound proteinuria. Six months after discontinuing lamivudine she remained clinically well, her urinalysis showed 0.04 g of protein per 24 hours, and there was microscopic haematuria. Hepatitis B DNA rose to >2000 pg/ml, indicating continued active viral replication. A repeat renal biopsy showed multiple electron dense deposits which had been

incorporated into the lamina densa with fragmentation of the latter, consistent with a membranous glomerulonephritis stage II/III. She has evidence of hyperfiltration with a glomerular filtration rate of 163 ml/min/1.73 m² as determined by ⁹⁹Tc DTPA clearance.

The ideal treatment for hepatitis B associated membranous nephropathy in children is yet to be determined. There is one retrospective analysis of six studies comprising a total of 82 children that showed 60% complete remission 12 months after the diagnosis, 7.3% renal failure, 2.4% end stage renal failure, and 30% persistent disease.² Steroid therapy should not be used as it does not appear to be beneficial, and the steroids may enhance viral replication in mononuclear cells.³ The average duration of proteinuria is 30 months.⁴ We believe that treatment with lamivudine in this case likely suppressed the virus and resulted in early remission of clinical nephrotic syndrome; however, the subsequent rebound in viral load and renal biopsy results probably indicates loss of viral suppression, leading to the subclinical relapse. It is unknown at this time if the strain of hepatitis B has developed resistance to lamivudine. Effective viricidal agents may be needed to prevent relapses of hepatitis B induced membranous glomerulonephritis. Finally, further work is needed to investigate the efficacy of this treatment in a larger cohort and to establish guidelines about the duration of such therapy.

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PCD or not PCD

In response to the leading article on primary ciliary dyskinesia (PCD)¹ and the commentary by Dr Andrew Boon, we write as clinicians with an interest in PCD who work in general paediatrics and neonatology.

We agree with Dr Boon that the identification of an uncommon medical disorder from the large number of children presenting with common symptoms and signs is a major challenge for the general paediatrician. We also support the view that it is undesirable and certainly impractical to refer every child with recurrent episodes of cough, rhinitis, and serous otitis media for further investigation.

However, we believe that the aim of the editorial by Professor C O'Callaghan and Dr A

Bush was to provide information on subtle differences in the clinical presentation of PCD to help us differentiate these patients from those with common non-specific childhood respiratory problems. For example, it is uncommon for a term infant to be admitted to a neonatal unit with significant respiratory concerns following a vaginal delivery but common in infants with PCD. We performed an as yet unpublished questionnaire survey of individuals belonging to the PCD support group which identified that 47% had been admitted to a neonatal unit with unexplained respiratory problems following a normal vaginal delivery. Rhinitis is also very rarely seen in normal neonates but is extremely common in patients with PCD. Other subtle clues increasing the likelihood of PCD are the characteristic of the cough and middle ear problems especially the development of persistent otorrhoea after tympanostomy tube insertion.

There is of course no doubt that a cheap reliable screening test would significantly help promote early diagnosis of PCD but it is not yet on the horizon. A detailed history especially of the neonatal period will help those working in neonatology or general paediatrics to highlight the patient that should be referred for further investigations including cilia studies.

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Hazards in the epidemiological study of sudden infant death syndrome

The study of Platt and Pharaoh, confirms the increased risk of SIDS in twins compared with singletons.¹ They point out that a major component of that higher accrued risk is that twins tend to be of low birthweight. Their finding that like-sex twins are at no greater risk than unlike-sex twins adds to the substantial evidence concerning the very limited role of genetic susceptibility for SIDS, and the rarity of recurrence in siblings of victims.²

The authors illustrate the gratifying fall in the number of SIDS during the six years of their 1990s study. As the number of infants categorised each year as SIDS in England and Wales comes nearer to that of 200, so it becomes more important for those involved in epidemiological studies to be sure that the categorisation (i.e. the diagnosis) is correct.

I refer to infants who, a few years after they have been categorised as SIDS, have been re-assessed, usually because of a subsequent child being abused or killed, and, in the course of court proceedings, findings are made that