Another case of HBV associated membranous glomerulonephritis resolving on lamivudine

Connor and colleagues (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, 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 iodohippurate 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. Steroid therapy should not be used as it does not appear to be beneficial, and the steroids may enhance viral replication in mononuclear cells. The average duration of proteinuria is 30 months. We believe that treatment with lamivudine in this case likely suppressed the viral load 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 virucidal 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.

**References**


**PCD or not PCD**

In response to the leading article on primary ciliary dyskinesia (PCD) 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 believe that the view that it is undesirable and certainly impractical to refer every child with recurrent episodes of cough, rhinitis, and a minor unexplained 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 not 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 cough and middle ear problems especially the development of persistent otitis media after tympanostomy tubes.

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.
the previous infant(s) were killed by the parent, rather than dying of natural causes. Currently, there does not seem to be a mechanism for correcting the national childhood mortality statistics when later, correct diagnoses are made. For instance, in the 1990s, I am aware that at least 20 infants who were initially categorised as SIDS, but who in later years, after extensive child protection investigations, were deemed to have been killed, usually by smothering. Colleagues will know of other cases: the true number will be higher. It is unfortunate that the official statistics do not seem to be altered retrospectively, and remain a misleading figure for any research worker. I should point out that, since the policy of parental killing of which I am aware involves twins, the conclusions of Platt and Pharoah are more likely to have been strengthened rather than weakened by such false diagnosis. However, as the number of SIDS continues to fall, it will become ever more difficult for research workers to compare small subgroups of SIDS within national mortality statistics unless the statistics are revised retrospectively in response to later corrected diagnosis.

It is appropriate to warn of an additional hazard for research workers in this field. In the same issue of Archives there was an inter- view with an epidemiologist in Illinois about the possibility of a relationship between the smoking of cigarettes and the occurrence of SIDS. The article stated, ‘The epidemiologist in Illinois is concerned that smoking may be related to SIDS’. This is a very legitimate concern, and it is unfortunate that the article deliberately assumes that smoking is responsible for SIDS, rather than any possible biases in the study. The article then goes on to quote a study from the UK where the authors state that there is no evidence that smoking is associated with SIDS. This is a very important study, and it is unfortunate that it is not mentioned in the article. The article also fails to mention a study from the UK where the authors state that there is no evidence that smoking is associated with SIDS. This is a very important study, and it is unfortunate that it is not mentioned in the article.

In conclusion, SIDS is a complex and multifactorial condition, and it is important to continue to study the various factors that may contribute to its occurrence. It is also important to continue to study the possible biases in studies that have investigated the relationship between smoking and SIDS. It is hoped that further research will be conducted to clarify these issues.

References


PostScript

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