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 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 per 24 hours, and there was microscopic hematuria with a glomerular filtration rate of 163 ml/min/1.73 m² as determined by iohexol 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 69% 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 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 viroidal agents may be needed to prevent relapses of hepatitis B induced membranous glomerulonephritis. Further, finally 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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References

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 chronic 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 otitis media 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.2 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.3

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...
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 of 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 add that, since none of the cases involved parental killing of which I am aware involves twins, the conclusions of Platt and Pharaoh are more likely to have been strengthened rather than weakened by such false diagnosis. Hence, if 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 interesting article by epidemiologists in Paris concerning the possibility of vagal overactivity as a cause of sudden infant death.10 They referred to a “positive family history of SIDS”. A careful reanalysis of cases is essential, particularly for cases both within and outside of the relevant family. These cases are verified in considerable detail, mistakes may be made. In recent years I have been involved with families in which parents who have repeatedly denied that their child has invented the family history, have been proved to be involved. Such cases have provided to paediatricians, genetic counselling services, and to SIDS research workers, a false family history of SIDS—for instance, mother saying that two of her own siblings “died of SIDS”. Such statements invariably are taken at face value and become part of the medical history: they are included in family trees in the hospital notes, and they have been quoted and displayed in published research concerning SIDS, yet subsequent questioning of the relevant grandparent has revealed that no such infant deaths occurred. Presumably, the mother responsible for smothering or killing her child has invented the family history; either to gain more medical attention for her child, or as a cover to distract from her actions. It is not unrealistic to expect the extent of the contemporary investigation and pathological examination. In one of Professor Emery’s studies of infants initially categorised as SIDS, detailed re-assessment pointed to either a definite natural cause, or abuse, in two thirds of cases.11

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References


Use of inhaled corticosteroids in children

I read with interest the article Survey of adrenal crisis associated with inhaled cortico-steroids in children by Boyd1 and the accompanying editorial in the December issue of Archives.

In the reported cases, the children had been administered substantially (up to 5 times) higher than the GlaxoSmithKline (GSK) Core Data Sheet recommended Flutisolate dose of 400 mcg/day and use of fluticasone (FP) at such doses is certainly not endorsed by GSK. Within the recommended doses, there are a wealth of data from clinical trials concerning no cases of adrenal crisis and no evidence of increased corticosteroid use on growth in children.1,2 There are a number of recent studies in children which identified no cases of adrenal crisis and no evidence of increased corticosteroid use on growth in children. There is therefore no evidence of a relationship between excessive dosing and adrenal insufficiency in children.3 The results of the research by Boyd et al.4 should be reviewed in this context. Any conclusions about the relationship between excessive dosing and adrenal suppression should be made with caution. The increase in corticosteroid use in children is due to the increased use of high dose inhaled corticosteroids used at such high doses has the potential to cause systemic effects, and paediatricians should be encouraged to treat their patients using the lowest effective dose, down-titrating as appropriate.

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9 DIN-LINK Data, Compufile Ltd, [March 2002].


