Successful Treatment of Hepatitis B Virus Associated Nephrotic Syndrome With Oral Lamivudine in a Nigerian Child: A Case Report

by Taiwo A. Ladapo,1 Elizabeth U. Onifade,2 Afolabi E. Lesi,1 and Olufunmilayo A. Lesi3

1Department of Pediatrics, Lagos University Teaching Hospital, Lagos, Nigeria
2Children’s Unit, Friarage Hospital, North Yorkshire, UK
3Department of Medicine, Lagos University Teaching Hospital, Lagos, Nigeria

Correspondence: Taiwo A. Ladapo, Lagos University Teaching Hospital, PMB 12003 Idi- Araba, Lagos, Nigeria.
E-mail: <drteeladapo@yahoo.com>.

Summary
Hepatitis B virus is a well described cause of nephrotic syndrome (NS) worldwide, the typical lesion being membranous glomerulonephropathy. HBV associated NS has been successfully treated with intravenous alpha interferon (IFN), an anti-viral agent. In recent times there have been reports of treatment with lamivudine, an orally administered nucleoside analogue inhibitor of HBV DNA polymerase in Caucasian children. Data is however limited and its actual efficacy and safety in children is yet to be determined. We present the case of an 8-year-old Nigerian boy with NS and active hepatitis B virus infection. He went into remission 3 months after commencing oral lamivudine which he had for a year with no significant side effects observed. He remains in remission 3 years later. This, to our knowledge is the first report in literature of successful treatment in an African child.

Key words: nephrotic syndrome, hepatitis B, lamivudine, children.

Background
Hepatitis B Virus (HBV) is a well-known cause of nephrotic syndrome (NS) worldwide [1–3], being more prevalent in HBV endemic regions of the world. HBV associated NS has been successfully treated with alpha interferon (IFN) therapy in both children and adults in the past [4, 5]. In recent times, there have been few reports of successful treatment with lamivudine, a nucleoside analogue inhibitor of HBV DNA polymerase with less significant side effects when compared with IFN [6, 7]. Lamivudine’s efficacy in the treatment of HBV associated nephropathy in black children has however not been established and there is, presently, no consensus about duration of treatment. We would like to share our experience in an African child.

Case Presentation
M.A., an 8-year-old male child presented with an 8-week history of progressive generalized swelling and oliguria. He was found to have anarsarca, hypertension (140/90) and an enlarged liver. Urine dipstick showed 4+ protein, with urine protein excretion of 1490 mg in 24 h. He had microscopic haematuria. Serum cholesterol was 290 mg/dl, total protein 66 g/l, albumin 22 g/l. Renal function tests were normal. His clinical features were in conformity with the diagnosis of NS.

He was positive for hepatitis B surface antigen (HBsAg), HBV e antigen (HBeAg), had antibodies to hepatitis B core antigen, but none to hepatitis e antigen. HBV DNA copies was >10 million/ml. Liver enzymes were raised (ALT 36 and AST 34) and kidney biopsy showed membranous glomerulonephritis on light microscopy. His NS was therefore diagnosed as being secondary to hepatitis B virus infection. Human Immunodeficiency Virus (HIV) screening was negative.

Prior to availability of all results, M.A. had proved resistant to oral prednisolone. On review of his diagnosis, he stopped prednisolone and was commenced on oral lamivudine, 2.5 mg/kg/day with good effect. His hypertension was treated with enalapril. Outcome was impressive. By 10 weeks he had no further proteinuria, by 5 months, liver enzymes were...
normal and hepatomegaly had resolved. He required no further antihypertensives. He remained on lamivudine for 1 year and since discontinuation 3 years ago has remained in remission. Following treatment, seroconversion from HBeAg positive to negative had occurred and he had acquired anti HBeAg and anti HBsAg with persistence of HBsAg.

Discussion

In endemic areas, a causal relationship between hepatitis B virus (HBV) and NS has been well described [1–3], the distribution of nephropathy often in parallel with the geographical patterns of prevalence of HBV [4]. The findings of HBV DNA and RNA in the glomeruli of chronic HbsAg carriers with associated glomerulonephritides [8, 9] as well as remission of NS accompanied by clearance of HBV replication, provide indisputable evidence of the role of the virus in the aetiology of the disease [3, 7, 10]. The actual duration between acquisition of the infection and onset of glomerulopathy is unknown but chronic carriage of the virus is known to predispose to the development of glomerulonephritides while the risk of chronic carriage may be inversely related to the age of the patient at the time of the infection [11].

Though clinically indistinguishable from idiopathic NS [1, 3], HBV-associated NS has been characteristically associated with a histological finding of membranous glomerulopathy [2, 3], as in our patient. Membranoproliferative glomerulonephritis, mesangial proliferative glomerulonephritis and IgA nephropathy have also been described to a lesser extent [2, 4]. Crescentic, focal segmental glomerulosclerosis and minimal change disease have been described as probable incidental findings [4], but this remains to be substantiated in view of increasing reports to the contrary [9, 12].

Untreated, most cases of HBV-associated nephropathy undergo spontaneous, nevertheless, slow resolution with a small percentage [1–3] progressing to chronic kidney disease. Significant morbidity and mortality in those without remission however justifies the need for treatment. Remission of proteinuria parallels elimination of HBV antigens especially HBeAg along with acquisition of antibodies to HBsAg and HBeAg [1, 6, 7, 10] as in our patient.

HBV-associated nephropathy in both children and adults has been successfully treated with the antiviral drug interferon [2, 5, 13], and more recently lamivudine [6–7, 13–15]. In a recent meta-analysis of treatment options, corticosteroids were found to be of no benefit [13] while interferon and lamivudine were associated with significant reduction in proteinuria. However, of the 9 trials analysed, the only one involving treatment with lamivudine was in adults while the few reports of successful treatment with lamivudine in children were among Caucasians [6, 7, 15]. Limitations to the use of interferon include high cost, lack of oral formulations and side effects [10], make lamivudine preferable. An apparent concern about use of lamivudine may be resistance because of its use in the treatment of HIV infection but this has not been established. Clinical trials to determine its actual efficacy and optimal duration of treatment in children are recommended.

References