

# Accelerated Renal Atherosclerosis in Congenital Nephrotic Syndrome: A Silent Fatal Inevitable Event

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## ABSTRACT

Accelerated atherosclerosis and thrombosis can be common, rapid evolving as short as two years in consequence of severe proteinuria in infancy who had low reserve of thyroid hormone and hyperlipidemia. This case report recommends and insist on aggressive treatment of hypothyroidism and hyperlipidemia besides to albumin infusion and folic acid to prevent hyperhomocysteinemia due to hypothyroidism side effect. This case was an evidence that imbalance of serum albumin level as a porter of lipids and LDL level can be a predisposing factor for accelerated atherosclerosis in other organs needs to more investigation for approve.

**Key words:** Atherosclerosis, Nephrotic, Accelerated, Proteinuria, Congenital, Infant.

## INTRODUCTION

Congenital Nephrotic Syndrome (CNS) is a rare and severe disorder characterized by heavy proteinuria and edema in the first 3 months of life. Microscopic findings in CNS description include: Proximal and distal tubular ectasia with flattening of tubular epithelium, microcysts, hyaline casts, glomerulosclerosis, mesangial hypercellularity, occasional immature glomeruli with or without glomerulosclerosis, when renal failure begins interstitial fibrosis, global glomerulosclerosis and tubular atrophy will be prominent.<sup>[1]</sup>

## CASE REPORT

A boy diagnosed as CNS in first week of life was treated by albumin infusion, vitamin and mineral supplements, angiotensin converting enzyme inhibitors and ibuprofen who was candidated for renal biopsy after first of life when his laboratory showed renal dysfunction, his renal biopsy showed typical finding of CNS, besides to obstructed arterioles with thickening media layer and inflammatory cell infiltration, hyalinization and wall thickness cause to completely obstruction of small and medium sized arteriols (Figure 1,2) all can be due to accelerated atherosclerosis due to hypercholesterolemia (Triglyceride:430 Cholesterol:217 LDL:117 and hypothyroidism (TSH:15, T4:1.5), renal failure with severe uremia (urea: 237 mmol/litre, Creatinine:1.1 mg/dl) presentation and severe acidosis after age one obligate us to manage chronic renal failure and peritoneal dialysis at age of 18<sup>th</sup> month.

## DISCUSSION

It seems that renal failure in CNS patients occurs in the second year of life in both developed and developing area.<sup>[2,3]</sup> In fact the mechanisms of chronic renal failure in CNS partly depends on renal ischemia because of recurrent AKI due to decrease intravascular volume and accelerated atherosclerosis. Accelerated atherosclerosis in kidney disease has been attributed to several unique and novel risk factors that affect the innate and adaptive immune system. Repeated episodes of AKI might thus contribute to a more persistent proinflammatory state that not only participates in progressive renal dysfunction and CKD but is also more pro-atherogenic,<sup>[4]</sup> but accelerated atherosclerosis is beyond of these theories, it is a complex phenomenon depends on hyperlipidaemia that escalate the progression of glomerular injury, in part owing to accelerated atherosclerosis in the renal vascular system. The lipid nephrotoxicity hypothesis is another inciting factor for renal dysfunction was proposed more than three decades ago and proposes that hyperlipidaemia, in addition to proteinuria and hypoalbuminaemia, lead to adverse and injurious effects in kidneys may cause glomerulosclerosis. In fact the podocyte is the primary target of cellular injury in nephrotic syndrome. During hyperlipidaemia or extracellular matrix expansion, increase LDL trapping and oxidation especially under conditions of mesangial cell stress, such as inflammatory, mechanical or ischaemic injury. Fatty components taken up by mesangial cells, leading to their proliferation and the release of several hazardous cytokines. Fatty acids bound to albumin might be the main contributors to tubulointerstitial injury by lipotoxic effects of saturated fatty acids in proximal tubular cell injury.<sup>[5]</sup> Hypothyroidism is a well-known com-

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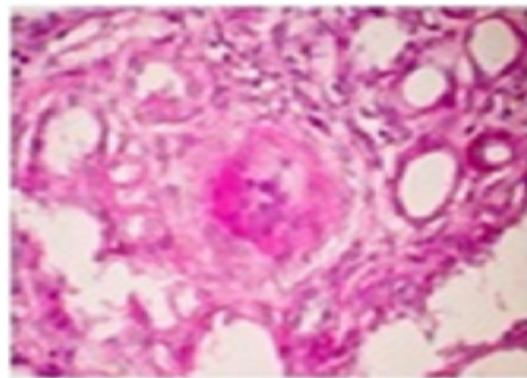
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**Figure 1:** An obstructed arteriole by thrombosis and thickening of medial layer thickness and inflammatory cell infiltration.



**Figure 2:** Increase amorph PAS positive, hyalinization and wall thickness and thrombosis cause to obstruction of small and medium sized arterioles completely.

plication of Nephrotic Syndrome (NS), a common feature of primary and secondary glomerular diseases and comprises loss of protein in the urine and increased urinary excretion of thyroid hormones and thyroxine-binding globulin.<sup>[6]</sup> Hypothyroidism not only make atherogenic lipid profile, diastolic hypertension and impaired endothelial function but recent studies suggest that hypothyroidism is associated with the emerging risk factors for atherosclerosis such as hyperhomocysteinemia and an increase in C-reactive protein level. Thyroid hormone also has direct anti-atherosclerotic effects by blood vessel dilatation, production of vasodilatory molecules and inhibition of angiotensin II receptor expression and its signal transduction.<sup>[7]</sup> Thrombosis is another frequent complication of Nephrotic Syndrome (NS), most frequently occurs in the earlier months of diagnoses though it may happen at any time during the course of NS, venous thromboses are common in NS but arterial thromboses are relatively rare. Venous thromboembolism is thought to be related to the degree of proteinuria and hypoalbuminemia while arterial thromboembolism is related to the presence of traditional risk factors for atherosclerosis.<sup>[8]</sup> This case show arteriole thrombosis is a finding that can be seen in a complex of atherosclerosis, hyperlipidemia, hypothyroidism and losing of coagulation factors by urine in severe NS.

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## CONFLICT OF INTEREST

The author declares no conflict of interest.

## ABBREVIATIONS

**LDL:** Low density lipoprotein; **CNS:** Congenital nephrotic syndrome; **TSH:** Thyroid stimulating hormone; **AKI:** Acute kidney injury; **CKD:** Chronic kidney disease.

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