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Editorial

# Neurological complications in nephrotic syndrome – Could they be prevented?

Nephrotic syndrome (NS) as the most common glomerular disease in children with an incidence of 1 in 50.000 children per year, usually presents between 2 and 5 y of age. Minimal change NS will be diagnosed in 80% of them and a good treatment response to steroids is expected in the majority of cases, restoring normal renal function.[1] So, a long term prognosis seems quite favorable.

However, although rare, during the nephrotic state neurological complications may occur, most often cerebral sinus venous thrombosis (CSVT) with or without parenchymal lesions. The majority of cases with CSVT only, would be successfully treated with anticoagulants with no longterm sequelae; but 18% of cerebral thromboembolic (TE) events in NS will manifest as arterial ischaemic strokes resulting in more or less serious lifelong neurological deficits.[1–3]

Another uncommon neurological complication in NS is posterior reversible encephalopathy syndrome (PRES) caused by localized brain angioedema. It presents acutely with sudden headache, seizures, visual disturbance, transient loss of consciousness, hypertension, diagnosis is confirmed by MRI.[4] Immediate antihypertensive treatment usually improves clinical symptoms and resolution of MRI brain hyperintensities follows within the next few months.[3,4]

In this issue, Stabouli and colleagues address these important complications providing a thorough review of all published cases.[3] The question remains: how can a patient with higher risk for neurological complications be recognized early in the course of NS in order to benefit from preventive treatment?

The incidence of thromboembolic events in children with NS is low, around 3%, in comparison to adults with NS, where the incidence is 25%; in both groups higher incidence is found in steroid resistant forms and during relapses of NS.[1,2]

The pathophysiology of TE is multifactorial: first, an individual may carry a genetic predisposition to TE such as single nucleotide polymorphisms associated with thrombophilia, for example congenital antithrombin deficiency etc. Secondly, the NS itself represents a prothrombotic condition due to changes in the plasma hemostatic protein content. This is due to glomerular loss of proteins involved in the inhibition of systemic hemostasis such as antithrombin and the active free form of protein S with a molecular mass of 69 kD similar to albumin. However, studies of free protein S have not demonstrated low levels of free protein S showing the complexity of the up-regulation.[1] On the other hand plasma concentration of procoagulant proteins with higher molecular weight, such as fibrinogen, factors V and VIII are markedly elevated. Also plasma concentration of a2-macroglobulin (725 kD) and lipoprotein (a) (500 kD), which are important inhibitors of fibrinolysis, are increased.[1,2] The result of all these changes in NS is diminished fibrinolytic activity counterbalanced with enhanced prothrombotic activity.[1] It is known that during the phase of severe proteinuria there is a 3.4-fold higher risk of venous TE, hypovolemia being additional trigger.[1,2]

Thirdly, among the acquired TE risk factors we should not forget central venous catheters and drugs. Steroid-resistant NS patients are at higher risk than steroid-sensitive NS patients.[1] Antiphospholipid antibodies as a co-morbidity in secondary NS are triggers leading to repeated renal vein thrombosis and later to recurrent arterial ischemic strokes.[5]

In summary, with optimal management of NS and early detection of additional prothrombotic risk factors we should aim to identify those patients at highest risk for thromboembolism and target them for prophylactic therapy. Any potential adverse effects (i.e., anticoagulant-related bleeding) need to be carefully balanced against the expected benefit of TE prevention.

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