Differential CR1 Expression in Adult and Paediatric Age Groups of Patients with Minimal Change Nephrotic Syndrome

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Dear Sir,

The kidney is very vulnerable to the deposition of immune complexes (ICs) due to its strategic position as well as its function as a filtration barrier for most immune material. A hypothesis relating the cause and onset of the minimal change nephrotic syndrome (MCNS) with an abnormal immune response has been proposed [1, 2]. MCNS is characterised by an absence of morphological evidence of renal damage, but reports indicate an abnormal T cell function. An increase in the population of total activated T cells with a specific T suppressor cell increase and T helper cell decrease was observed in paediatric MCNS [3]. The impaired T cell function involved a decreased response to mitogens/polyclonal activators [4]. It could be reversed by adding normal human serum, hence suggesting the presence of certain inhibitory factors in the diseased serum [5]. The involvement of serum in improving the status of the disease was supported by a report indicating a role for C3, the third component of the complement system, as a cofactor in antigen-dependent T cell activation [6].

Apart from the hepatic complement synthesis, the glomerulus in itself has a potential for complement synthesis through its epithelial, mesangial and endothelial cells. The tissue is controlled by differential regulation [7, 8]. It may prove destructive as in IC-mediated glomerulonephritis and yet it may be useful in solubilization of ICs thus enabling their clearance. The protective role of complement entails the binding of C3b, a split product of C3 generated on stimulation by ICs, C1q, C4 and C2. The binding of C3b to ICs (opsonisation) facilitates their uptake through complement receptors on phagocytic cells [9]. The glomerular endothelial cells take up the opsonised ICs through C3b receptors (CR1) on their membranes from the vascular compartment and capillary wall and release them into urinary spaces. Thus, an efficient C3b as well as CR1 expression would facilitate an effective processing. CR1 also has a regulatory role as it is a cofactor for factor-I-mediated cleavage of C3b to C3bi and hence helps in the release of ICs from E surface and transferring it to fixed macro-phage system.

We have studied the CR1 expression on MCNS biopsies of 16 patients, including 10 paediatric biopsies and 6 adults, using monoclonal mouse anti-human CR1 and FITC-anti-mouse IgG. We observed a normal and granular staining pattern of the receptor in all adult (average age: 40 years) MCNS biopsies, with an intense +2 fluorescence in the capillary walls and +1 intensity in the mesangium (fig. 1a). The Bowman's capsule and the vascular pole stained negative for the receptor. As expected, there was no trace of IC deposits in all these cases.

In contrast, paediatric MCNS biopsies showed a different, interesting finding. All the biopsies from children (average age: 5.4 years) showed a complete absence of the receptor (fig. 1b) and resembled expression in IC-mediated glomerulonephritis and systemic lupus erythematosus biopsies.

Such an absence of receptor expression in children may indicate an inability of the tissue to synthesise complement as well as a reduced hepatic complement protein synthesis. The latter was normal as evidenced by a normal receptor expression on erythrocytes. Hence, tissue synthesis of complement is impaired. The tissue synthesis is both constitutive and cytokine dependent [10], and a differential expression is found within the tissue itself which may be regulated by many local factors, including cytokines which are known inducers of complement synthesis [11, 12]. Other evidences implicate an auto-antibody to the receptor, a blockade by IC as well as a proteolytic cleavage of CR1 [13,14].

It is known that complement levels are usually normal in MCNS, but there are studies indicating low C3, factor B and D levels which may have developed due to the disease and are manifested by proteinuria [15]. A reduced CR1 expression with a subsequent appearance in the urine has been shown [16], pointing to the loss of receptors being an acquired phenomenon developed during the course of the disease [17]. The pattern obtained during remission could be of help in providing further support for the hypothesis and requires further investigation. A follow-up of the patients at a later stage would also help to establish whether the reduced receptor expression is a phenomenon restricted to the paediatric age group.

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Fig. 1. a Photomicrograph of an adult MCNS glomerulus showing an intense fluorescence for CR1 in capillary walls and mesangium. × 200. b Photomicrograph of a glomerulus from a paediatric biopsy showing a reduced fluorescence for CR1. ×200.

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