SUMMARY

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Nephrotic syndrome is the most common chronic renal disease of childhood. It is a bewildering disease with many mysteries in the etiology, pathogenesis, clinicopathological and therapeutic correlates. A vast diversity of immunological phenomenon have been described in MCNS. Evidence for classic mechanism of immunologic injury has been lacking.

The present study was designed to investigate the peripheral blood T-cell subset (CD4 and CD8), IL-2R expression and IL-2 production as T-cell activation criteria in patients with MCNS.

Sixty children were the subjects of this study. The children were divided into equal 4 groups:

G I: Patient with NS in 1st presentation.

G II: Patient with NS in remission.

G III: Patient in relapse.

G IV: Normal healthy control.

To avoid steroid effect, the patient in 1st presentation and relapse were before prednisone treatment and in remission group were, at least, 4 weeks off prednisone.

The results of this work were the following:

(1) The total lymphocytic count showed that the 1st presentation and relapse groups were significantly lower than remission and control groups.

(2) The percent of $CD4^+$ cells was significantly higher in the 1st presentation and relapse groups compared to the remission. While all three groups were significantly lower than the controls.

(3) The percent of $CD8^+$ cells showed no statistical significant difference among the 4 groups.

(4) The percent of $CD25^+$ cells (IL-2 receptors) was significantly high in 1st presentation and relapse groups compared to the remission and control groups.

(5) The mean serum IL-2 was significantly lower in all three groups compared to controls but significantly higher in the remission group compared to the 1st presentation and relapse groups.

(6) In the 1st presentation group: $CD4^+$ cells % didn't show any significant correlation. $CD8^+$ % showed a significant positive correlation with the total serum protein and total lymphocytic count. CD25+ % and IL-2 level showed a significant negative correlation with blood Hb concentration.

(7) There is no significant correlation in remission and relapse groups with any of the studied parameters.

(8) In the control group $CD4^+$ % showed a significant negative correlation with systolic blood pressure and protein in the urine. CD8+ % showed a significant negative correlation with systolic blood pressure. Both $CD25^+$ % and IL-2 level didn't show any significant correlation.

(9) There is a significant high $CD25^+$ / creatinine (serum) ratio in the 1st presentation and relapse compared to remission and control groups. There is also a significant lower IL-2 / Creatinine (serum) ratio in the 1st presentation and relapse compared to remission and control groups values.

(10) It was found that only serum IL-2 had the possibility of predicting 1st presentation from controls with total prediction of 86.67% and predicting the relapse from control with a total prediction of 93.3%.

From all previous finding a hypothetical scenario of the etiopathogenesis of MCNS could be suggested as follow in short: A viral infection affects patients and presented to naïve T-cell without proper co-stimulation. This will prevent the IL-2 production leading to cellular apoptosis which will reduce total lymphocytic count. There is excess IL-2R as it requires only T-cell receptor ligation. $CD8^+$ cell does not show a high increment in their number because they need excess IL-2.

There is predominant differentiation of T-helper (T_H) into T_H2 more than T_H1. Activated T_H1 cells, although not in large number, secrete different mediator affect renal vascular permeability, activate endothelial damage and induce macrophage differentiation in bone marrow. Activated macrophage act as APCS to stimulate T-cell and produce several harmful cytokine as IL-1B, INF-α.

Remission could occur due to activity of T_H2 to arrest and reverse the immunological damage and that is why remission occurs in some patients without the use of corticosteroid. Prednisone regulates expression of many genes, with a net anti inflammatory effect that counteract the damage in MCNS.

Presence of memory T-cell recruited in different lymphoid tissues will lead to an easy relapse when ever it affected by the original offending virus.

d) Induction of apoptosis in lymphocytes by increasing endonucleases leading to nuclear destruction of lymphocytes.

e) Diminishes number of monocytes to less than 50 cells/ul leading to diminished number of macrophages. (141)

So the remission could be occur due to the activity of T_H2 cells to reverse and arrest the immunological damage and that is whey remission occurs in some patients without use of corticosteroids. If this is not sufficient then the use of corticosteroids will lead to remission in steroid sensitive patients.

The presence of memory T-cells recruited in different sanctuaries in the lymphoid tissues will lead to an easy relapse of the NS whenever affected by the original offending virus.