Monocyte Function in Idiopathic Nephrotic Syndrome in Childhood

KISHIRO NAGATA, YOSHIHIRO TAKAHASHI, SHINOBU WAGA, MAKOTO FUJITA, TADAYUKI KURONUMA* and RYUZO AYOYAMA†

Department of Pediatrics, Hirosaki University, School of Medicine, Hirosaki 036, *Iwaki Hospital, National Sanatorium, Pediatrics, Namioka 038-13, and †Hirosaki National Hospital, Pediatrics, Hirosaki 036

NAGATA, K., TAKAHASHI, Y., WAGA, S., FUJITA, M., KURONUMA, T. and AYOYAMA, R. Monocyte Function in Idiopathic Nephrotic Syndrome in Childhood. Tohoku J. Exp. Med., 1981, 135 (4), 413-417 — The monocyte function in 2-15 year old patients with idiopathic nephrotic syndrome (INS) in childhood was studied in reference to the phagocytosis of sensitized red blood cells and NBT reduction. The monocyte function was found to be increased in fresh cases of INS. In the case of refractory INS not responding to steroid treatment, the monocyte function was normal or tended to be low.

— monocyte; phagocytosis; NBT; reticuloendothelial system; idiopathic nephrotic syndrome

Not much is known about the etiology of idiopathic nephrotic syndrome. There is no doubt, however, that immune system is concerned with INS. Recent reports have also mentioned abnormality in serum immunoglobulin level (Giangiacomo et al. 1975), T cell dysfunction (Wissermann et al. 1977; Nagata et al. 1979), the appearance of plasma inhibitory factors (Tomizawa et al. 1979) and detection of circulating immune complex (Abras et al, 1979) in minimal change group. It is quite possible that the function of reticuloendothelial system (RES) plays an important role in INS. However, the study on the function of RES in INS is scanty. Various ways to assess this RES function are available, but they are not always easy to practice. In order to evaluate the function of monocyte, a component part of RES, we conducted a study using peripheral blood on the phagocytosis and nitroblue tetrazorium (NBT) reduction of monocyte in INS children.

MATERIALS AND METHODS

INS children aged from 2 to 15 years were divided into a group that responded to steroid treatment and a group that didn't. The group responding to steroid treatment, moreover, was subdivided into four: fresh cases which had not been treated with steroid, cases of relapse, cases of incomplete remission, and cases of complete remission.

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Reprint request should be addressed to Dr. K. Nagata, Dept. of Pediatrics, Hirosaki Univ. School of Medicine, Hirosaki, Japan.
These cases were mostly of the minimal change group. On the other hand, the group non-sensitive to steroid treatment had membranoproliferative glomerulonephritis (MPGN) and mesangial proliferative glomerulonephritis.

Phagocytosis was studied by a method using antibody-coated red blood cell (RBC). That is, RBC of type O was washed with physiological saline solution four times. A 5% RBC suspension and anti-D serum (Dade Co.) were mixed in equal amount, the mixture was allowed to stand at 37°C for 30 min and washed with Hanks balanced salt solution (BSS) three times to make a 5% RBC suspension. Mononuclear cell was prepared by centrifugation of 2 ml of heparinized peripheral blood on a Ficoll metrizoate gradient and washed the cell with Hanks BSS once. The suspensions of RBC and mononuclear cell were mixed each in equal amount, and the mixtures were allowed to stand at 37°C for 60 min. One drop of the mixture was taken on a slide glass. The slide glass was again allowed to stand at 37°C for 60 min and then washed gently with Hanks BSS. Monocyte accounted for 50 to 80% of the cells adhered. After fixation in methanol and Giemsa staining, the percentage for RBC-phagocytosing monocyte was calculated.

The NBT reduction was studied by the method of Park et al. (1968). In preparing NBT reagent, equal amounts of 0.2% NBT/physiological saline solution and 0.15 M phosphate-buffered saline solution (PBS—pH 7.2) were mixed. This mixed solution and the suspension of mononuclear cell were mixed in equal amount, and the mixture was allowed to stand at 37°C for 30 min. One drop of this mixture was taken on a slide glass. The slide glass was allowed to stand at 37°C for 60 min and washed with Hanks BSS. After fixation in methanol and Giemsa staining, the percentage for formazan-positive monocytes was calculated.

RESULTS

The value of phagocytosis (Fig. 1) tended to be high in fresh cases, was high in some of the incomplete remission cases, was normal in the complete remission cases, tended to be low in the group not responding to steroid treatment, and was high in some cases and low in others even during steroid administration.

NBT reduction level (Fig. 2) was high in fresh cases, tended to be high in cases of relapse and cases of incomplete remission, and was almost normal in cases of MPGN and mesangial proliferative glomerulonephritis which had proteinuria and were also poorly responsive to steroid treatment. One case with slightly elevated NBT reduction values in steroid non-sensitive group is the one studied at a time when symptoms of MPGN presented themselves. The figure shown by this case was low compared with fresh cases in the group responding to steroid treatment. There was a positive correlation between phagocytosis and NBT reduction (Fig. 3).

DISCUSSION

In the present study, the phagocytic activity of monocytes with respect to the IgG Fc receptor was investigated in idiopathic nephrotic syndrome concerning its

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Fig. 1. Phagocytosis of anti-D coated RBC by monocytes in NS.
Normal range 8.5±5.9% (mean±s.d.). o, no proteinuria, no steroid therapy; Δ, no proteinuria, on steroid therapy; ●, proteinuria, no steroid therapy; ▲, proteinuria, on steroid therapy.

Fig. 2. Nitroblue tetrazorium dye test of monocytes in NS. Normal range, 12.2±2.5% (mean±s.d.).
stage and response to steroids. The IgG Fc receptor (Lo Buglio et al. 1967) as well as the C3 receptor (Huber et al. 1968) is one of the essential receptors of monocytes. Evaluation of monocyte function was also investigated by the use of NBT reduction test in the present study. NBT reduction test is useful in evaluation of neutrophil function regulated by the hexose monophosphate shunt activity (Pachman et al. 1973).

The increased activity of both phagocytosis and NBT reduction of monocytes was observed in the active stage as well as in the initial stage of idiopathic nephrotic syndrome. In these two stages, monocyte function is possibly activated by a common stimulating factor. No increase in monocyte function even in the active stage in some cases which showed poor response to steroids especially in MPGN was observed in the present study. Monocyte function does not directly indicate the functional activity of the systemic RES. Drivas et al. (1976) observed increased phagocytosis in the RES in the active stage of renal diseases by the use of the clearance of iodinated human serum albumin.

It is recently speculated that monocytes can also present the phagocytic activity against immune complexes and/or macromolecules even after monocytes have entered mesangium. Sheinman et al. (1978) reported the findings of marked decrease in both actomyosin and fibronectin in mesangium in progressive mesangial proliferative glomerulonephritis, indicating that the glomerular mesangium function has close relation to the progression of renal disease. These findings and speculation reported in the recent literature well consist with the results observed in the present study. Further studies of the function of the systemic RES in relation to the function of peripheral monocytes and macrophages and of localized glomerular mesangium are necessary.
References


