Papillary Necrosis and the Antinuclear Factor

Masayuki ENDOH, Yasuo NOMOTO, Yasuhiko TOMINO, Hideto SAKAI, Shigeru ARIMORI and Yasuhide MURAKAMI*

Department of Internal Medicine, School of Medicine, Tokai University
*Department of Urology, School of Medicine, Tokai University
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The cold-reacting antinuclear factor, specific to kidney tissues, was detected transiently in serum specimens from a diabetic patient during an episode of papillary necrosis. Determination of the cold-reacting antinuclear factor is suggested as being useful in evaluating the degree of destruction in kidney tissues.

(Key Words: Papillary Necrosis, Antinuclear Factor, Diabetes Mellitus, Pyelonephritis)

INTRODUCTION

The antinuclear factor (ANF) is an autoantibody detected in serum samples from patients with autoimmune disorders such as systemic lupus erythematosus. Although conventional warm-reacting ANF is not detected in primary glomerular diseases, Nomoto and Sakai(5) reported that cold-reacting ANF specific to kidney tissues was observed in patients with chronic glomerulonephritis. In this study, we detected cold-reacting ANF in serum specimens from a diabetic patient during an episode of papillary necrosis and excretion of the necrotic tissues into the urine.

CASE REPORT

A sixty-two-year-old woman was admitted to the Tokai University Hospital on May 29, 1978, because of progressive weakness and fluid retention. There was no remarkable history in the past, and the weakness and fluid retention appeared incidiously. On physical examination, she was found to have ascites with an enlarged liver and pitting edema in the lower extremities.

Laboratory studies demonstrated a hemoglobin level of 8.8g/dl, a white blood cell count of 12,000/mm³ with granulocytosis, and a thrombocyte count of 190,000/mm³. The serum glucose was 250mg/dl, urea nitrogen 35mg/dl, creatinine 2.5mg/dl, glutamic oxaloacetic transaminase 35IU/L, glutamic pyruvic transaminase 18IU/L, lactic dehydrogenase 183IU/L, alkaline phosphatase 180IU/L and bilirubin 1.0mg/dl.

There was 1+ proteinuria, and the urine sediment contained 10-50 red blood cells and 100 white blood cells in the high power field. A urine
culture showed $10^7$/ml of Escherichia coli. The oral glucose tolerance test revealed a markedly impaired glucose tolerance with poor response of endogenous immunoreactive insulin. A liver scintigram showed hepatomegaly with increased uptake in the spleen and bone marrow without space occupying lesions. The general condition of the patient was improved by administration of insulin, antibiotics and diuretics. However, she developed pyelonephritis repeatedly with continuous gross hematuria from December 20 to 27, 1978 (Fig. 1). On the seventh day of the hematuria, a piece of necrotic tissue was excreted into the urine, and was found to be a necrotized papilla by microscopic examination (Fig. 2).

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**Fig. 1** Clinical course and laboratory data showing changes in fever, status of bacteria, serum creatinine levels and titers of cold-reacting A.N.F.

**Fig. 2** Light microscopic examination of the renal papilla excreted in the urine; necrotized tubules frequently appear as empty spaces. H&E × 6.
Cold-reacting ANF in sera was detected for two weeks following the episode of excretion of the necrotized papilla. The immunoglobulin classes of the cold-reacting ANF in this patient were IgM with the titer of 1:40 and IgG with the titer of 1:20; results were negative for IgA. The staining pattern was "speckled" (Fig. 3). Conventional warm-reacting ANF was never detected in this patient throughout the study period.

**Fig. 3**  The speckled pattern of nuclear staining detected transiently in a serum specimen from the patient. (immunofluorescent microscopy, original magnification ×200)

**DISCUSSION**

The antinuclear factor (ANF) was observed in a diabetic patient during an episode of papillary necrosis. A conventional clinical test of ANF (warm-reacting ANF) was performed as follows: serum specimens were incubated with chicken erythrocytes or human leukocytes at 37°C for 30 minutes, followed by staining with FITC-conjugated anti human γ-globulin antisera. Cold-reacting ANF studied in this report was detected by the incubation of serum samples with kidney tissues at 4°C overnight. Mouse kidneys, as well as normal human kidneys, could be used as substrates (5). This cold-reacting, kidney specific ANF did not react with spleen tissue and leukocytes, and reacted weakly with liver tissues.

Papillary necrosis occurs in patients with diabetes mellitus(1, 4), pyelonephritis(1, 4), analgesic nephropathy(3) and sickle cell anemia(2). This patient showed diabetes mellitus and pyelonephritis, but she had never been administered any analgesics or DNA-sensitizing drugs. It is postulated that cold-reacting ANF was developed in this patient following extensive destruction of papillae, because the cold-reacting ANF emerged only for a short period after the excretion of necrotized papilla into the urine.

Although the nephritogenic significance of cold-reacting ANF is not known, the detection of kidney specific cold-reacting ANF may be useful for the evaluation of tissue damage in patients with chronic pyelonephritis.
Fig. 4 Retrograde pyelogram taken after the excretion of necrotized papilla showing the typical "ring-shadow" of renal papillary necrosis.

REFERENCES