

The Serum Pregnancy Associated α_2 -Glycoprotein Level in Patients with Nephrotic Syndrome^{*}

Noriaki YORIOKA, Akira HIRABAYASHI, Makoto KOBAYASHI,
Kenichiro SHIGEMOTO, Jyotaro HATA, Shunji TOI,
Shinji MIYAMORI, Toshihide TOYOTA, Sayuri OKUSHIN,
Hidemasa MARUISHI, Michio YAMAKIDO and Yukio NISHIMOTO

The 2nd Department of Internal Medicine, Hiroshima University School of Medicine, 1-2-3,
Kasumi, Minami-ku, Hiroshima 734, Japan

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ABSTRACT

The serum concentration of pregnancy associated α_2 -glycoprotein (α_2 -PAG) was determined by Laurell's immunoelectrophoresis in 15 male nephrotic patients and 89 healthy males. The results were as follows.

- 1) The nephrotic males showed significantly higher values than the healthy males.
- 2) Study of changes in serum α_2 -PAG in the nephrotic patients showed a relationship between α_2 -PAG value and clinical course. This suggests that this value is useful in the observation of the clinical course of nephrotic patients.

INTRODUCTION

α_2 -PAG is a glycoprotein with a molecular weight of about 300,000 which was isolated and purified by Bohn³⁾. α_2 -PAG can be found in only minute volumes in healthy persons, but the serum concentration increases markedly with pregnancy. There are reports that the serum concentration also increases in the presence of malignant tumors^{1,2,8)}, and interest has been focussed upon it as a tumor marker during recent years^{5,9,10)}.

However, there are very few reports on the behavior of α_2 -PAG in renal disease patients. As we have noted interesting findings of serum α_2 -PAG during the clinical course of nephrotic patients, they are reported herein.

MATERIALS AND METHODS

1) Materials

The subjects are 15 males with primary nephrotic syndrome whose ages range from 15 to 55 (mean 29.3±13.5). The histological type

consisted of minimal change 7 cases, membranous glomerulonephritis 4 cases, membranoproliferative glomerulonephritis 2 cases, focal glomerulosclerosis 1 case and mesangial proliferative glomerulonephritis 1 case. The controls consisted of 89 healthy males, whose ages ranged from those in their second to seventh decades. The specimens used for determination was serum.

2) Methods

Serum α_2 -PAG was determined by Laurell's⁷⁾ immunoelectrophoresis. First, an agarose gel plate which contains antihuman α_2 -PAG rabbit serum was prepared, and small wells were made in the gel plate. Next, standard serum (Behringwerke Co.) and test serum were placed into the wells and electrophoresis was performed. The standard curve was prepared on the basis of the length of the precipitation line, and the α_2 -PAG concentration of the test serum was sought. The sensitivity of measurement by this method is 0.5 mg/dl.

^{*} 頼岡徳在, 平林 晃, 小林 誠, 重本憲一郎, 幡城太郎, 東井俊二, 宮森真治, 豊田敏秀, 奥新小百合, 丸石秀正, 山木戸道郎, 西本幸男: ネフローゼ症候群患者における血清 Pregnancy associated α_2 -glycoprotein の動態

RESULTS

1) Serum α_2 -PAG value of nephrotic patients (male)

Study was made of serum α_2 -PAG value in nephrotic patients, and in those in whom a precipitation line was not observed on Laurell's⁷⁾ immunoelectrophoresis were classified as negative and those in whom the line was present were considered positive. The results showed that 10 out of 15 patients (66.7%) were positive, while in the healthy control group only 23 out of 89 (25.8%) were positive. Thus, the positive rate was significantly higher in the nephrotic patients ($p < 0.01$).

Also the respective determined values of

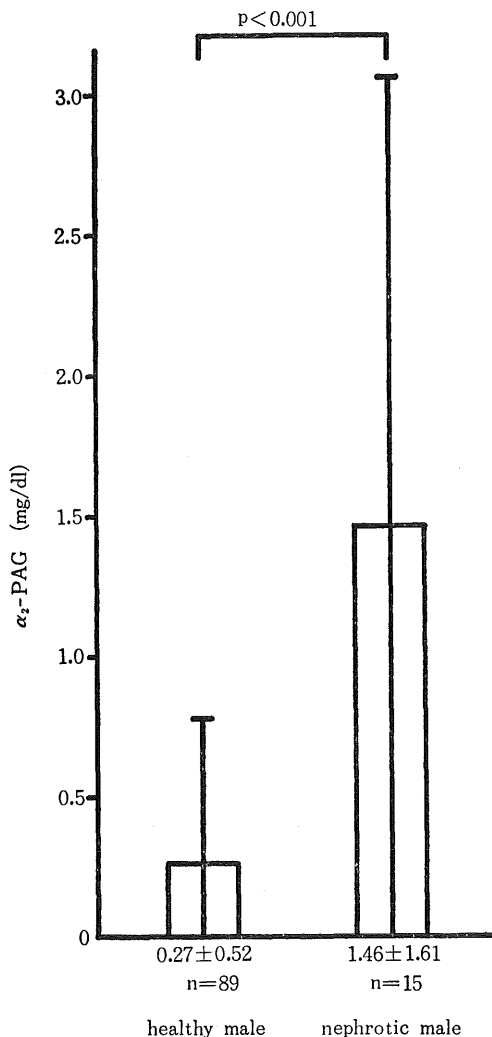


Fig. 1. Serum α_2 -PAG values in healthy males and nephrotic male patients

1.46 ± 1.61 mg/dl for male nephrotic patients were significantly higher than the 0.27 ± 0.52 mg/dl for healthy males ($p < 0.001$) (Fig. 1).

2) Changes in serum α_2 -PAG value in male nephrotic patients

A review will be made of changes in the serum α_2 -PAG values and clinical course in two male nephrotic patients.

Case 1 (Fig. 2)

The patient was 15-year-old, male who noted edema of the face on December 30, 1981, and was admitted to a hospital on January 4, 1982 under the diagnosis of nephrotic syndrome. At time of admission, severe proteinuria and hypoproteinemia were noted, but proteinuria became negative with steroid therapy. However, as proteinuria increased when the steroid dose was reduced, he was referred to our hospital on April 16 of the same year.

On admission, he was found to have facial edema and acne, but his blood pressure was normal and no other abnormal physical findings were observed. Laboratory test findings showed daily urinary protein was 4.4 g indicating severe proteinuria. However, total serum protein was 6.2 g/dl, total serum cholesterol 247 mg/dl, renal function by GFR 131 ml/min, RPF 450 ml/min, Ccr 124 ml/min and PSP 15' 30%, which were all within the normal range. Histological study revealed the minimal change. On the other hand, his serum α_2 -PAG value at time of admission was a high 3.1 mg/dl. Thereafter, he was treated with steroids, immunosuppressive agents, and steroid pulse therapy, and was discharged 3 months later after attaining a complete remission.

His serum α_2 -PAG value gradually decreased to 1.4 mg/dl and further to 0.7 mg/dl, and eventually together with his proteinuria and other clinical data which also improved, all became negative.

Case 2 (Fig. 3)

The patient was a 22-year-old, male, university student who became aware of facial edema on October 23, 1980. Severe proteinuria was pointed out at the Health Management Center of the University, and he was admitted to a hospital under the diagnosis of nephrotic syndrome. His proteinuria disappeared with the administration of steroids, but as it recurred when the dose was reduced, he was admitted to our department on July 3, 1981.

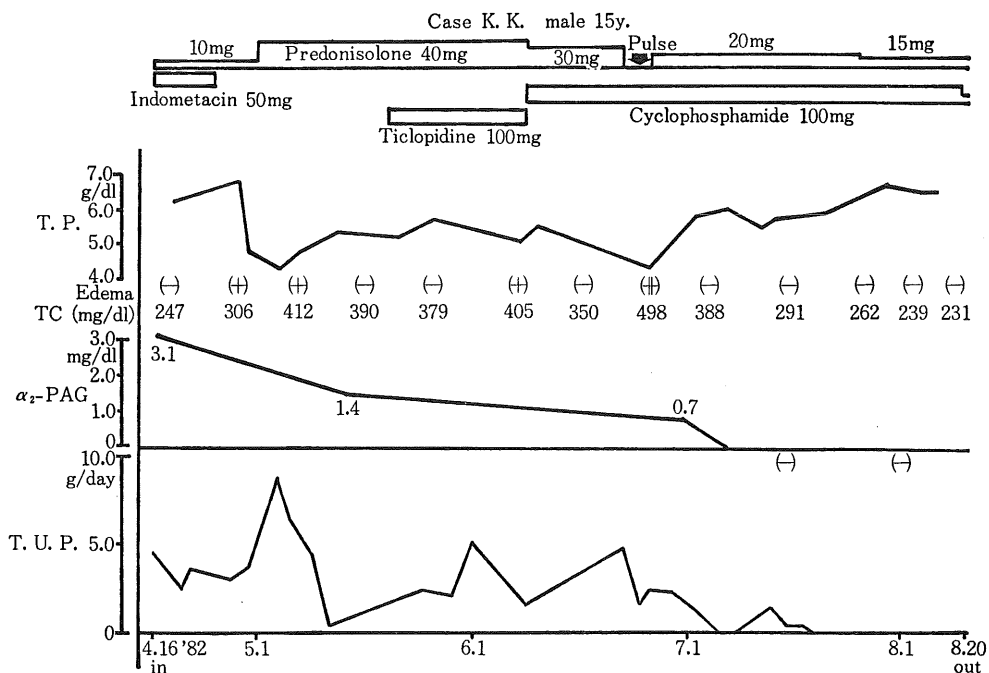


Fig. 2. Changes in serum α_2 -PAG value in case 1

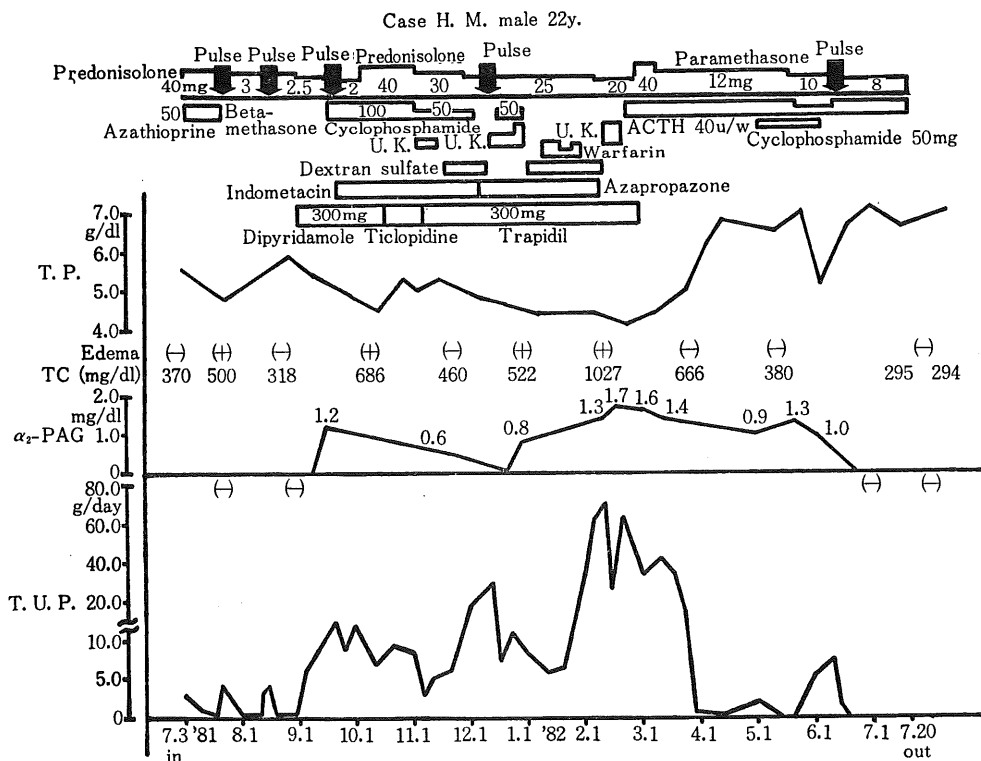


Fig. 3. Changes in serum α_2 -PAG value in case 2

The physical findings noted at time of admission were slightly elevated blood pressure of 144/90, moon face and acne, but there were no other remarkable findings. Laboratory findings on admission were proteinuria 3.5 g/day, total serum protein 5.5 g/dl and total serum cholesterol 370 mg/dl. Histological test showed the minimal change. His proteinuria became negative temporarily with steroid pulse therapy, but severe proteinuria recurred. His α_2 -PAG value which was negative at time of admission, increased to 1.2 mg/dl and reached the maximum value of 1.7 mg/dl. The proteinuria at the time was 70 g/day. None of the various methods of treatment attempted proved effective, but when the steroid pulse therapy was repeated in June 1982, a complete remission was attained. At the same time, his serum α_2 -PAG value also became negative.

DISCUSSION

In 1971, Bohn⁹⁾ succeeded in isolating four types of pregnancy associated proteins. That is, 1) human placental lactogen (HPL) and 2) pregnancy specific β_1 -glycoprotein (SP₁) which are both said to be pregnancy specific, and 3) pregnancy associated β_1 -glycoprotein (SP₂) and 4) pregnancy associated α_2 -glycoprotein (SP₃, α_2 -PAG) which were found also in minute volumes in healthy individuals. Of these, it is reported that the serum concentration of α_2 -PAG increases in the presence of malignant tumors and in inflammatory diseases^{1,2,4,8)}. Particularly, attention is being focussed upon it as a tumor marker in malignant tumors^{5,9,10)}. However, reports on its behavior in renal diseases are limited to that of Horne et al.⁶⁾ who found the serum concentration to be elevated in renal disease patients with severe proteinuria and our report¹¹⁾ of elevated values in chronic hemodialysis patients.

Thus, we made a review of its behavior in patients with primary nephrotic syndrome, particularly males. As a result, it was found that male nephrotic patients had a significantly higher value than healthy males. Also review was made of its relationship with the clinical course of two nephrotic patients in the minimal change group. It was observed that the α_2 -PAG value decreased and became negative with improvement of the clinical course. On the basis of the above, it is considered that deter-

mination of serum α_2 -PAG is useful in the diagnosis and follow-up of the clinical course in nephrotic patients.

We plan to study the mechanism responsible for inducing elevation of serum α_2 -PAG in nephrotic patients and its relationship with histological type.

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