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Serum Immunosuppresive Acidic Protein in Renal Cell Carcinoma

T. Ueda

Department of Urology, Faculty of Medicine, Kyushu University, Fukuoka, Japan

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Summary. Serum immunosuppresive acidic protein (IAP) was determined in 45 patients with renal cell carcinoma (20 preoperative and 25 postoperative) and 12 healthy adults. The mean values of serum IAP in patients with renal cell carcinoma of low stage (566.3 ± 197.7 μg/ml) and high stage (936.9 ± 208.8 μg/ml) were statistically higher than those of controls (368.8 ± 84.5 μg/ml). Positive rate of IAP levels was found in 58.3% and 100% of patients with low stage and high stage, respectively. The mean value of serum IAP was 756.4 ± 361.0 μg/ml in patients with metastases, while patients without metastases had a value of 434.7 ± 170.9 μg/ml. There was a statistically significant difference between the two populations. These results suggest that IAP levels appear to provide a useful diagnostic and follow-up marker in renal cell carcinoma patients.

Key words: Immunosuppresive acidic protein, Renal cell carcinoma, Tumor marker, Clinical stage, Distant metastases.

Introduction

Recently, many biological tumor markers have been evaluated in urologic cancers [2]. However, useful markers for renal cell carcinoma have not been established clinically. Serum immunosuppresive acidic protein (IAP) found in serum of Ehrlich ascites cancer in mice rises significantly in patients with cancer and has immunosuppresive activity [7]. IAP has been estimated as a marker in testicular, colorectal and ovarian cancers [3, 5, 6]. In the current study, the clinical advantage of IAP as a diagnostic and follow-up marker for renal cell carcinoma was evaluated.

Materials and Methods

IAP was evaluated in 20 patients with renal cell carcinoma and in another 25 patients with or without metastases following nephrectomy for renal cell carcinoma from August, 1984 to February, 1985. The 17 women and 28 men ranged in age from 39 to 79 years. Three patients had serial determination of IAP at frequent intervals after nephrectomy. IAP values were also evaluated in 12 healthy adults as controls. Clinical staging of renal cell carcinoma was performed according to Robson's classification [4]. Clinically stage was divided into two groups, that is, low stage (I and II) and high stage (III and IV), respectively.

Blood samples drawn from patients and healthy adults were centrifuged at 3,000 r.p.m. for 10 min. Serum was stored at −20 °C until analyses were performed. IAP values were assayed by single radial immunodiffusion method (Kitazato Biochemical Lab., Tokyo, Japan). In this study, the normal range was under 500 μg per 1 ml serum. Statistical analysis of the results was performed using Student t-test.

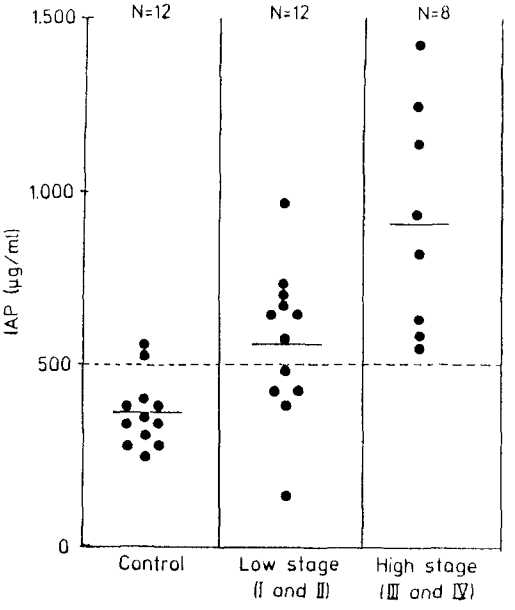

Fig. 1. Serum IAP levels in controls and patients with renal cell carcinoma

Results

1. Correlation Between Clinical Stage and IAP

The IAP levels of renal cell carcinoma patients stratified according to clinical stage and controls are shown in Fig. 1.

Table 1. Correlation between serum IAP levels and stage of renal cell carcinoma

Stage	Total No. Pts.	Serum IAP levels (μg/ml) (mean ± S.D.)
Low stage (I and II)	12	566.3 ± 197.7[a,c]
High stage (III and IV)	8	936.9 ± 208.8[b,c]
Control	12	368.8 ± 84.5[a,b]

a,b,c $P < 0.01$

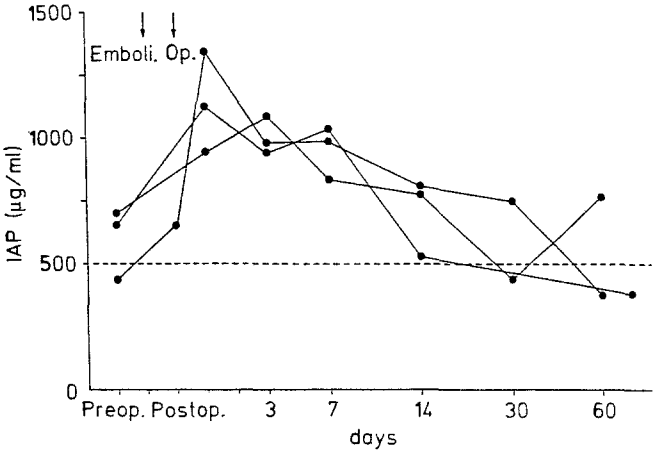

Fig. 2. Postoperative changes of serum IAP levels in patients with renal cell carcinoma (Stage I)

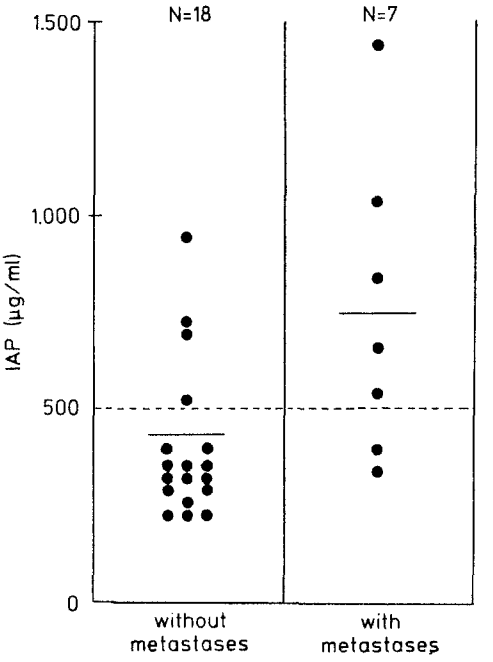

Fig. 3. Serum IAP levels in patients with or without metastases of renal cell carcinoma following nephrectomy

Table 2. Correlation between serum IAP levels and metastaic organs of renal cell carcinoma following nephrectomy

Case	Age	Sex	IAP levels (μg/ml)	Metastatic organs	Postop. duration
1	43	M	355	Lung	7m
2	51	M	405	Lung	2y 10m
3	73	M	520	Lung	1y 10m
4	72	M	665	Lung, bones, brain, skin	3y 4m
5	76	M	830	Bones	5m
6	74	M	1,050	Lung, bones	2y 7m
7	47	M	1,450	Bones	1y 11m

Table 3. Correlation between serum IAP levels and metastases of renal cell carcinoma following nephrectomy

Metastases	Total No. Pts.	Serum IAP levels (μg/ml) (mean ± S.D.)
Absence	18	434.7 ± 170.9[a,c]
Presence	7	756.4 ± 361.0[b,c]
Control	12	368.8 ± 84.5[a,b]

a n.s.
b,c $P < 0.01$

Two of 12 healthy adults (16.7%) had elevated IAP levels while 7 of 12 patients (58.3%) with low stage disease and all of patients (100%) with high stage disease had a high level of IAP. The mean level of IAP was 368.8 ± 84.5 μg/ml in the controls. The mean levels of IAP in patients with low stage disease and high stage disease were 566.3 ± 197.7 μg/ml, 936.9 ± 208.8 μg/ml, respectively (Table 1). The IAP levels of low stage disease and high stage disease were significantly higher than those of controls ($P < 0.01$). Moreover, there was statistically significant difference between the IAP levels in high stage disease and those of low stage disease ($P < 0.01$).

2. Correlation Between Postoperative Course and IAP (Fig. 2)

Two of 3 patients with Stage I had elevated IAP value prior to nephrectomy. IAP levels were elevated for 7 days postoperatively and then fell progressively to normal levels within 4 or 8 weeks after nephrectomy in all of patients. However, levels were elevated at 8 weeks in one patient.

3. Correlation Between Postoperative Metastases and IAP

In 4 of 18 patients (22.2%) without metastases IAP levels were elevated while high IAP levels were observed in 5 of 7 patients (71.4%) with metastases (Fig. 3). Distant bony metastases were found in 4 of 5 patients with high IAP levels (Table 2). The mean IAP levels in patients without and with metastases were 434.7 ± 170.9 μg/ml and 756.4 ± 361.0 μg/ml, respectively (Table 3). The difference between the two popullations was statistically significant ($P < 0.01$). There was no statistically significant difference between IAP levels of patients without metastases and the levels in control samples.

Discussion

IAP is a acidic protein with a molecular weight of 50,000 and isoelectric focusing at pH 3.0 [1]. It was found not only in large quantities in the sera of cancer patients, but in small amounts in the sera of healthy persons. This protein has the immunosuppresive activities to the phytohemagglutinin-induced lymphocyte blast formation and mixed lymphocyte reaction in vitro. Tamura et al. have established a new method of analyzing IAP, which differs from normal α_1-acid-glycoprotein, and reported that a definite increase of IAP could be found in 67% of all cancer patients [7]. On the other hand, there are no reports on the evaluation evaluated of IAP in renal cell carcinoma patients. We evaluated the clinical use of IAP as a marker of renal cell carcinoma.

There was a statistical difference between the mean value of IAP in renal cell carcinoma patients and the value in controls, even for low stage disease. Moreover, the positive rate of IAP levels was 58.3% in low stage disease and 100% in high stage disease. From these results it is suggested that the IAP level is a useful diagnostic marker in renal cell carcinoma. A clear relationship was found between the value of IAP and clinical stage. In other words, it would be possible to utilize to IAP to determine the extent of renal cell carcinoma.

The result of the postoperative course of IAP levels showed that the value of IAP becomes reliable at 4 or 8 weeks after nephrectomy. It is noteworthy that the IAP level is effected by operation, inflammation and collagenoses.

There was a significant difference between the IAP levels in patients with metastases and those in patients without metastases. Seven patients had distant metastases and the IAP level was elevated in 5 (71.8%). These results suggest that IAP determination indicates the presence of metastases in postoperative patients. However, the IAP assay produced two false-negative (2 of 7) and 4 false-positive results (4 of 18) in postoperative patients. Also, 5 false-negative (4 of 12) results were observed in preoperative patients with low stage disease. Further investigation of IAP will be necessary to make IAP a more accurate marker in renal cell carcinoma. Two of 7 patients with metastases to the lung had normal IAP levels. On the other hand, 4 of 5 patients with high IAP levels had bony metastases. These results may indicate that the IAP level is affected by the site of metastasis.

In conclusion, IAP determinations may be useful for a diagnostic and follow-up marker of renal cell carcinoma. The measurement of IAP is highly recommended in renal cell carcinoma patients.

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Dr. T. Ueda
Department of Urology
Faculty of Medicine
Kyushu University
Maedashi 3-1-1, Higashiku
812 Fukuoka
Japan