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SHORT COMMUNICATION

Total IgA and IgG in Sera of Patients With Different Primary Malignancies*

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The concentrations of total serum IgA and IgG of 267 patients with different primary malignant tumors were measured by ELISA. Total serum IgA increased by 30% to 40% in patients with malignancies associated with mucous membranes (nasopharyngeal, gastrointestinal and bronchial carcinomas), while the change in total serum IgG was negligible. Although, the changes in Ig level could be influenced by many host factors, these data call attention to the potential indicative role of total serum IgA levels. Further studies are required to establish links between serum IgA levels and stages of tumor growth or tumor progression in order to use these values as prognostic factors. (Pathology Oncology Research Vol 2, No1–2, 66–68, 1996)

Key words: IgA; IgG; malignant tumors

Introduction

Immunoglobulin A (IgA) is the first, most efficient protector and the major Ig synthesized along the mucosal surfaces. IgA can also be produced by plasma cells anywhere in the body.[7,13]

The local active form, secretory IgA (SCIgA), is effective against bacterial and viral infections, and, presumably, against tumor antigens. Circulating SCIgA loses the secretory component (SC) which recognizes the receptors on the biliary epithelial cells of healthy liver.[7] Attempts to evaluate serum concentrations of IgA indirectly by measuring the concentrations of serum SC failed to give relevant results.[1,4,8]

It is known that IgA synthesis is stimulated in tissues with primary malignant tumors.[7] The increase of total serum IgA is accompanied by high levels of serum carcinoembryonic antigen (CEA) and α-fetoprotein (AFP).[5,14] In patients with colon carcinoma, the serum levels of secretory IgA were related to Duke's stage.[8] An important effect of IgA is downregulating tumor necrosis factor α (TNFα) and interleukin-6 (IL-6) production, whereas IgG has no such effect.[15] The use of specific IgA and IgG antibodies as "screening markers" in malignancies associ-

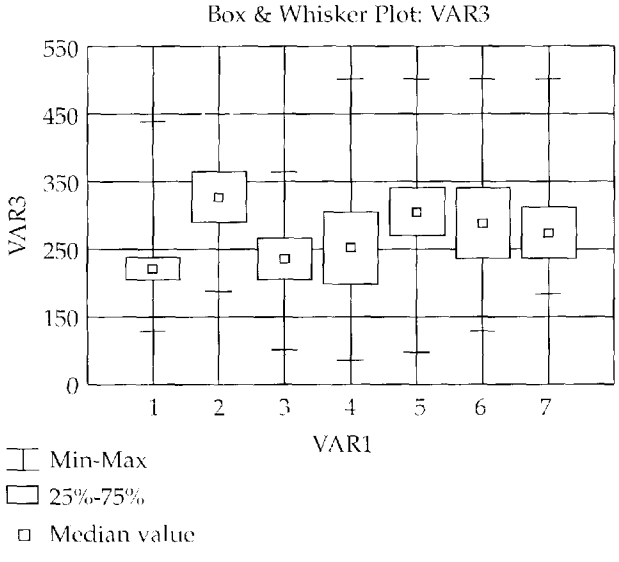

Figure 1. Values of serum IgA concentration measured by ELISA (Kruskal-Wallis test: $p < 0.001$) in different groups of patients. The bars show the minimum/maximum values, the big boxes the values between 25%-75%, and the small boxes the median value.

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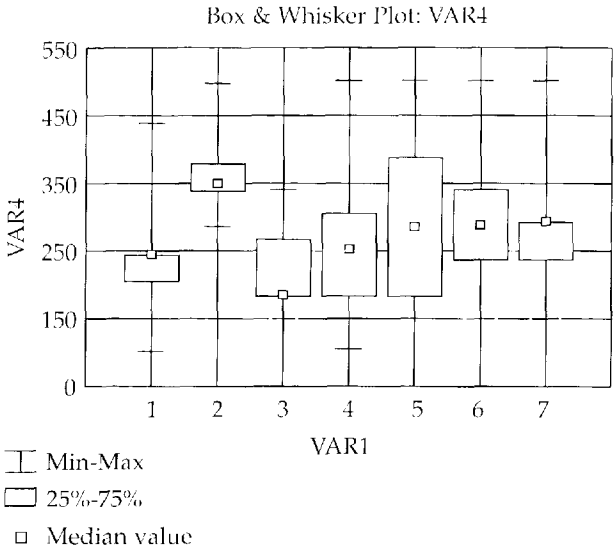

Figure 2. Values of serum IgA measured by RID. ($p < 0.001$). Symbols see on Fig. 1.

ated with viral infections was suggested in nasopharyngeal carcinomas,[3,10,11] and in carcinomas of the uterine cervix.[6,9,12]

Based upon these observations in this study we measured the concentrations of total IgA and IgG in the sera of patients with primary tumors of different organs.

Materials and Methods

Sera were obtained from 267 patients aged from 25 to 70 years of both sexes, as soon as they were admitted to the clinic. Pathological diagnosis was provided later. The samples were grouped according to the location of primary malignant tumors: 1. control (clinically healthy adult persons of the same population: 38 men and 20 women); 2. nasopharyngeal area: 67 samples; 3. uterus/ovary: 27 samples; 4. breast: 68 samples; 5. lung: 55 samples; 6. gastrointestinal tract: 28 samples, and 7. skin: 16 samples.

All sera were tested for IgA and IgG by double gel diffusion on 1.5% agarose, and then stored at –20°C. Detection of serum IgA and IgG concentrations was performed by ELISA. Radial immunodiffusion (RID) was used as a control during the development of the ELISA.

Levels of significance for comparison between patients' and control groups were estimated using the Kruskal-Wallis test. The average increase (compared to control) of total serum IgA in relation to the average increase of total serum IgG in each patient group was evaluated. An index (I) was introduced to measure the increase of IgA % relative to the increase of IgG %. [I = IgA% – IgG%/IgA%].

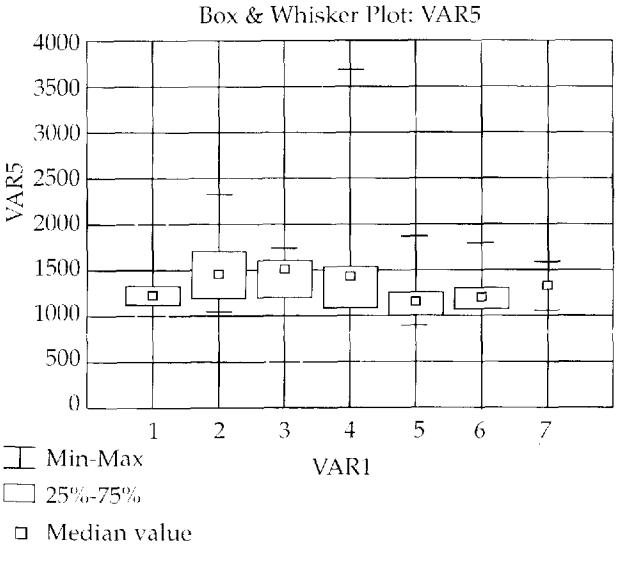

Figure 3. Values of serum IgG concentration measured by ELISA. ($p < 0.1$). Symbols see on Fig.1.

Results and Discussion

The concentrations of serum IgA and serum IgG measured by ELISA are shown on *Fig.1*, by RID on *Fig.2*; and values for IgG measured by ELISA on *Fig.3*.

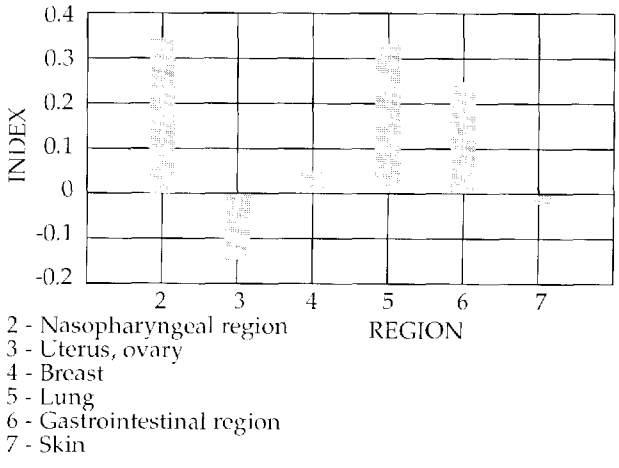

Figure 4. Changes of Ig index (I = IgA%-IgG%/IgA%) in the different patient groups.

Fig.1 and *2* show remarkable increase of serum IgA concentration in certain groups of patients, while the change of serum IgG level is minimal *(Fig.3)*. The percent values for IgA and IgG of the controls are given as an index of expression on *Fig.4*. The index was positive in malignancies derived from mucous membranes (nasopharyngeal, bronchial, GI tract), but not in others (breast, uterus/ovary, skin).

Although all of these data could be influenced by many host factors (e.g. liver function, Ig expression by non-tumorous tissues) the changes call attention to the potential indicative role of total serum IgA level. Again,

further studies are required to establish any link of IgA levels to stages of tumor growth or to tumor progression in order to use them, essentially, as prognostic factors.

References

1. *Brooks JJ and Carolin SE:* Immunoreactive Secretory Component of IgA Human Tissues and Tumors. Am J Clin Pathol 82:660-665, 1984.
2. *Brown WR and Kloppel TM:* The liver and IgA. Immunological, Cell Biological and Clinical Implications. Hepatology 9:763-789, 1989.
3. *Chan CK, Mueller N, Evans A, Harris NL, Comstock GM, Jellum E, Magnos K, Orentreich N, Polk BF and Vogelman J:* Epstein Barr virus antibody patterns preceding the diagnosis of nasopharyngeal carcinoma. Cancer Causes Control 2:125-131, 1991.
4. *Delacroix DL, Jonard DP and Vaerman JP:* Serum IgM-bound secretory component (SIgM) in liver diseases. Comparative molecular state of the secretory component in serum and bile. J Immunol 129:133-138, 1982.
5. *Gong YZ, Zhang XY and Chen XT:* In vitro synthesis of SIgA and CEA and their relationship in gastric cancer tissue. Chung-Hua-Chung-Liu-Tsa-Chin. 10:184-187, 1988.
6. *Kanda T, Onoda T, Zanma S, Yasugi T, Furuno A, Watenabe S and Kawana T:* Indepedent association of antibodies against human Papilloma virus type 16 E1/E4 and E7 proteins with cervical cancer. Virology 190:724-776, 1992.
7. *Keren FD:* Mucosal IgA elaboration. Critical Reviews in Clinical Lab Sci 27:158-176, 1989.
8. *Kvale D, Rognum TO and Brandtzaeg P:* Elevated Levels of Secretory Immunoglobulins A and M in Serum of Patients With Large Bowel Carcinoma Indicate Liver Metastasis. Cancer 59:203-207, 1987.
9. *Lehtinen M, Leminen A, Kuoppala T, Tikkainen M, Lehtinen T, Lehtovirta P, Punonen R, Veterinen E and Pavonen J:* Pre- and posttreament serum antibody responses to HPV 16 E2 and HSV 2 ICP8 proteins in women with cervical carcinoma. J Med Virol 37:180-186, 1992.
10. *Littler E, Baylis SA, Zeng Y, Conway MJ, Mackett M and Arrand JR:* Diagnosis of Nasopharyngeal Carcinoma by Means of Recombinant Epstein-Barr Virus Proteins. Lancet 337:685-689, 1991.
11. *Lung ML, Lam WP, Sham J, Chay D, Yung-Sheng Y and Guo HY:* Detection of prevalence of the "f" variant of Epstein-Barr virus in southern China. Virology 185:67-71, 1991.
12. *Radhakrishna PM, Balaram P, Hareendran NK, Bindu S, Abraham T, Padmanabham TK and Nair MK:* Immune reactive proteins as prognostic and clinical markers in malignant cervical neoplasia. J Cancer Res Clin Oncol 115:583-691, 1989.
13. *Russell MW, Lue C, Van den Wall Bake AWL, Moldoveanu Y and Mestecky J:* Molecular heterogenity of human IgA antibodies during an immune reponse. Rev Clin Exp Immunol 87:1-6, 1992.
14. *Smyslova VN:* Possibilities of Prognosis in Cancer of the Transverse Colon and Rectum using CEA, AFP, and Immunoglobulins A, M, and G. Vopr Oncol 33:42-48, 1987.
15. *Wolf HM, Fisher MB, Pnebringer H, Smastag A, Vogel E and Eibl MM:* Human serum IgA downregulates the release of inflammatory cytokines (tumor necrosis factor – alfa, interleukin-6) in human monocytes. Blood 83:1278-1288, 1994.