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RESEARCH ARTICLE

ESTIMATION OF SOME CYTOKINES IN IRAQI PATIENTS WITH CANCER NEWLY IDENTIFIED

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Abstract

Immunological activating cytokines are important during immune response against cancers. In Iraqi population, the detection of immune status of cancer cases has been studied rarely, although the incidence of chemical and radiation pollution have been reported often. This study concerned with breast and large intestine cancers (the most common cancer types), and aimed to evaluate some critical cytokines in the immune defense mechanisms towards cancer to configure a view about their initial immune response. The cytokines estimated were IL-2, IL-12 and γ-IFN using ELISA technique and serum samples of newly identified patients with these types of cancers. Results: The findings showed that most of our cases had low levels of the estimated cytokines. We concluded the low levels of IL-2, IL-12 and γ-IFN can be consider as predisposing factors for developing cancers in breast and large intestine.

Introduction

Cancer is the well-known deadly disease all over the world. In Iraq, this disease incidence increased due to chemical and radiation pollution (Al-Hamdany, 2011). Breast and large intestine cancers are the most common types recorded in the previous three decades in Iraq (Iraqi Center Board, 2008).

Both humoral mediated immunity (HMI) and cellular mediated immunity (CMI) are involved in the immune response against cancer. But, CMI is more significant. Innate immunity recognizes the cancerous cells that arose and destroy them by the help of both macrophages and natural killer (NK) cells. These events are intermediated by many cytokines; γ-IFN which activates and enhances MHC I and II, macrophages, antagonizes IL-4 activities and inhibits the proliferation of T-helper2 (Th2). This important cytokine is produced by T-helper 1 (Th1), T cytotoxic (Tc) and NK cells (Delves et al., 2006).

The Cytokine IL-2 produced by Th1, activates monocytes and macrophages and induces the proliferation of activated T and B lymphocytes. In addition, induces the Tc and NK cells cytotoxicity to kill tumor cells. The IL-12 sources are monocytes, macrophages, denderic cells and B-cells. It is a critical cytokine for Th1 differentiation, induces proliferation of Th1 and production of γ-IFN by Th1, Tc and NK cells, also enhances NK and Tc cytotoxicity, moreover their basic action as an antiviral activity; the same as other family members proteins do (Kuby, 2003).

The above mediators have the major role in pushing forward the immune response towards cancer cells, whether were strongly or weakly immunogenic tumors (Edgar, 2004; Manoj et al., 2011).This study aimed to evaluate the levels of these critical cytokines in cancer patients newly identified with cancer tumors to configure a view about their initial immune response against cancer.

MATERIALS AND METHODS:

- **Cases:**

This study involved cancer patients newly identified with no medication or treatment taken before. A total of (23) patients including both genders; (14) females and (9) males; aged (18-70) years, not smokers, no clinical signs of any infection or consequence. The cases restricted with breast and large intestine cancers and were identified by specialized physicians in the Hospital of Baghdad medicine Town in Baghdad and

after biopsy histopathological diagnosis. This study started and accomplished during 2013, (between January and May).

- **Samples:**

A total of (23) blood samples were collected from the above cases and put in clean tubes, serum was separated from them according to Lewis (2006). Serum samples were kept after labeling in Eppendrof tubes and stored in freezer until use (Mckenzie, 2004).

- **Cytokines estimated in this study:**

Three cytokines were involved in this study; all of them were estimated using special kits for ELISA (Sandwich indirect method) provided by R&D Systems company, USA.

- **Gamma –Interferon (γ-IFN).**
- **Interlukine-2 (IL-2).**
- **Interlukine-12 (IL-12).**

Each cytokine estimation was carried out using serum samples and according to the work steps in the leaflets enclosed in each kit.

- **Statistical Analysis:**

Statistical analysis included mean calculations only and according to SAS system (2000).

RESULTS:

The results showed that breast cancer was more frequent than large intestine cancers. Also, ages (32-55) years were the predisposed ages to induce these cancers.

Concerning cytokines, the obtained values for **γ-IFN** were between (0.155- 0.684 IU/ml) with a mean (0.453 IU/ml). No remarkable increase was recorded and most of the values were near the lower limit or less comparing with the normal dependant range (0.39-25 IU/ml) (Delves et al., 2006).

The estimated levels of **IL-2** were around the minimum limit and ranged (318-1042 pg/ml) with a mean (486 pg/ml). No elevation recorded in any case comparing with the normal dependant range (75-1200pg/ml)(Delves et al., 2006).

The resultant values for IL-12 estimation ranged between (55.6-404 pg/ml) with a mean (113.23pg/ml). No elevation recorded and the obtained values were lower or near the low limit according to the dependant normal range (29-3535 pg/ml)(Delves et al., 2006).

DISCUSSION:

According to results of Iraqi Cancer Registry (Iraqi Center Board, 2008), the breast cancer is at the top of most common ten cancer types in Iraq. This fact supports our result.

Concerning cytokines levels, collectively, most of our cases were suffering from diminished immune response. The suppression in CMI is very obvious according to the levels obtained. Since, CMI is the main defense mechanism against cancerous cells; these findings can give an explanation for cancer induction in those patients.

The scientist Tizard (2009), who stated the initial response against cancer, involves the enhancement cytokines production to regulate the immune response by Th1 activation. The authorsDelves et al., (2006), documented that all components of the immune system (non-specific and specific; humoral and cellular) can affect the growth and progression of a tumor. Macrophages and NK cells need to be activated before releasing their toxic content to the extracellular spaces between them and target cells (cancer cells) (Danso and Bacch, 2005).

Our results were in agreement with those ofTsavaris et al., (2002), they found that patients with low levels of immune activating cytokines suffer from developed breast cancer than others. Also, our finding are in consistent with those of Thery and Amigorena, (2002), since any defect in phagocytic cells activation will cause antigen presenting cells (APC) to be compromised in doing their function, and that is the same findings of Segal, (2005) too. Levels of cytokines can affect the feature of cancer in critical events, as stated by Xianfeng et al. (2012). Hence, successful immunotherapy against cancers mainly involves these cytokines, pointing to γ-IFN(Lee and Margolin, 2011).

The mixture of cytokines that is produced in the tumor microenvironment has an important role in cancer pathogenesis. Cytokines that are released can function to inhibit tumor development and progression. Alternatively, cancer cells can respond to host-derived cytokines that promote growth, attenuate apoptosis and facilitate invasion and metastasis, as suggested by Dranoff (2004).

The authors Demian et al., (2011) wereinvestigated the levels of γ-IFN in Egyptian breast cancer patients and found thatγ-IFN levels were diminished significantly and increased after administration of immunotherapy with IL-12, that is supporting to our results that under focus cytokines are working synergistically and their levels are in association.

In another hand, several researchers investigated the levels of IL-12 and IL-18 in serum and tissue samples of gastric cancer patients using ELISA test, they demonstrated that both cytokines were involved in

the development of intestinal type gastric cancer. In addition, IL-12 levels increased in patients with good inflammatory immune response with negative association with cancer stage and primary tumor regression (Diakowska et al., 2011). Also, the scientists Long and Raufman, (2011)had estimated IL-2, IL-12 and several other cytokines, they stated that in patients suffering from progressed colon cancer patients, these cytokines establish the initiation of innate immune response of cell-mediated response of adaptive immunity. Those studies may explain our findings that these cytokines were not elevated according to our results, since our patients were newly identified and the disease was in its initiation stage in most of our involved cases, and these cytokines levels increase during the progress of the disease. At the same time, low levels of these cytokines can lead to loss of control in cellular immunity to eliminate the cancerous cells before they succeed to induce the disease by fell down the body control of the immune system.

CONCLUSION:

As a conclusion; peoples with low levels of IL-2, IL-12 and γ-IFN cytokines are more predisposed to develop cancers in the breast or large intestine than others.

References

Al-Hamadany, W.S. (2011): Radiation Pollution in Cancer and other Diseases Using some Immunological and Clinical Parameters. Ph. D. Thesis. Dep. Microbio. Coll.Scien. Baghdad University.

Danso, M.A. and Bacch, E.M. (2005): Hematology and Oncology pearls. Elsevier mosby Publishing. USA, pp.118-157.

Delves, P.J., Martin, S.J., Burton, D.R. and Roitt, I.M. (2006):Roitt's Essential Immunology, 11th Edn, Blackwell publishing Ltd, pp. 361-387.

Demian, S.,Hamdy, M., Ali, I., (2011): The regulatory effects of interleukin-12 on interleukin-18 and interferon-γ production in Egyptian breast cancer patients. Alexandria J. of Med., 47: 283-290.

Diakowska, D., Grabowski, K., Nienartowicz, M., Szelachowski, P. and Markocka-Maczka, K. (2011):Serum and Tissue levels of Interleukin-12 and Interleukin-18 in intestinal type gastric cancer. J. GastroenterologiaPolska, 18(3): 103-108.

Dranoff, G. (2004): Cytokines in cancer pathogenesis and cancer therapy. J. Nature Reviews Cancer, 4:11-22.

Edgar, J.D. (2006): Immunology: Master Medicine, 1stEdn. Elsevier Churchill Livingstone Publishing, pp. 293-304.

Iraqi Cancer Board, (2008): Results of Iraqi Cancer Registry (1997-2008), Iraqi Cancer Board Pub. Iraqi cancer Registry Center, Ministry of Health.

Kuby, J. (2003): Immunology: Text Book, 3rdEdn. W. H. Freeman comp. New York, pp. 78-83.

Lee, S. and Margolin, K. (2011): Cytokines in Cancer Immunotherapy. J. Cancer, 3(4):3856-2893.

Lewis, S.M., Bain, B.J., Bates, I.,Dacie and Lewis,(2006): Practical Hematology, 10th, Elsevier publishing Ltd, pp. 76-83.

Long, T., and Raufman, J. (2011): The Diagnostic and Prognostic role of cytokines in colon cancer. J. Gastrointestinal cancer Target and Therapy, (1):27-39.

Manoj, L., Kalyani, M., Jyothi, K., Ganga, Bhavani, G. and Govardhani, V. (2011): Review of Brain and Brain Treatment.Internat.J.ofpharma. andBioScience, 2(1):468-477.

Mckenzie, S.B. (2004): Clinical Laboratory Hematology. Pearson Education, Inc. USA, pp. 245-265.

Segal, A.W. (2005): How Neutrophils kill microbes. J.Annu. Rev. Immunol, 23:197-223.

Statistical Analysis System (SAS).(2000): SAS/Stat user guide for personal computer. Release 6.12 SAS Institute. Inc. Cary. N.C. USA.

Thery, C. and Amigorena, S.(2002): The cell biology of antigen presentation in dendric cells.J.Curr.Opin. Immunol, 13:45-51.

Tizard, I.R. (2009): Veterinary Immunology: An Introduction. 8th Edn. Saunders Elsevier Inc. Publishing. USA, pp. 311-318.

Tsavaris, N., Kosmas, C., Vadiaka, M., Kanelopoulos, P. and Boulamatsis, D. (2002): Immune Changes in Patients with Advanced Breast Cancer Undergoing Chemotherapy with Toxanes. J. Cancer. Jul., (1): 21-27.

Xianfeng, L., Xueqin, YANG, Yuxin, YANG, Xianqing, G., Ling, L. and Dong, W. (2012): Evaluation of Serum Cytokines in Small Cell Lung Cancer and Its Clinical Significance. Chinese J. of lung cancer, 15(1):11-16.