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Survey of Intestinal Parasitic Infection in Leukemic Children and Evaluation of their Serum Immunoglobulins

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Abstract
Infection is one of the cardinal difficulties in the children with acute leukemia and is the leading cause of mortality among them. The prevalence of infection in these patients has several reasons including usage of cytotoxic agents, corticosteriods, broad consumption of antibiotics, duration of confinement in hospital, defective of cellular and humoral Immunity, neutropenia and dysfunction of neutrophils. Despite the fact that intestinal parasitic infection is a rather frequent finding and a health problem in developing countries, in our experience the incidence of helminthic and protozoa infections among children with leukemia was uncommon. Totally 141 patients with leukemia and 70 cases of control group were examined in a period of 12 months, which 40% and 2.8% of former and latter groups, had intestinal pathogen and non-pathogen parasites, respectively. When we compared the frequency of parasitic infection in the control group with the leukemic children, we found no significant difference. It is speculated that parasitic infections may uncommon in these children for numerous reasons such as immunologic and pharmacologic parameters.

Keywords: *Intestinal parasites, Leukemia, immunoglobulin*

Introduction
Leukemia is a heterogenous group of neoplasia, occurred due to malignant deformity of stem cells. It makes disorders in normal immunity system and hematopoiesis. Leukemia is the most prevalent malignancy in children below 15 years. A large number of children are afflicted yearly, and these little victims will die because of infection (1). Leukemia has been divided into two groups according to the type of involved cells, i.e. Myeloid and Lymphoid which based on clinical process it is divided to chronic and acute. Acute leukemia shows a rapid clinical process and posses no treatment, eventually causes die after some months, but chronic leukemia has a longer normal cycle (2). Acute Lymphoblastic Leukemia (ALL) is a disorder in children and young adults but Acute Myeloblastic Leukemia (AML) is seen in all ages. Natural B lymphocytes which exist in peripheral blood cells contain light and heavy chain immunoglobulins genes: CD_{21}, CD_{24} antigens and HLA (3). After antigenic stimulation, lymphocytes change to plasma cells, which have cystoplasmic immunoglobulins. Study on different types of infections in leukemic children has been subject of many investigations such as bacterial, viral and fungal infections. But the station of parasitic infection especially intestinal parasites is not obvious. So many studies have been done in the case of humoral immunity variation and IgG, IgA and IgM antibodies in leukemic children. In this study, investigation on intestinal parasites and humoral immunity variation in leukemic children has been challenged.

Materials and Methods
The project has been designed considering the nature of systemic leukemia and consumption of cytotoxic drugs in patients. Samples were collected from both case and control groups as follows:
1. Stool samples collected in formalin 10% from 141 children affected with ALL and AML.
2. 05 serum samples from aforementioned group.
3. 70 stool and serum samples from healthy control group. Sampling was done in Aliasghar hospital-in Tehran city. First, Specification of study group (sex, age, duration of disease etc, was documented in a questionnaire. Second, parasitologic examinations from both case and control group was done as follows: Watery samples were examined with preparation of direct smear and microscopically, while formed samples were examined with concentrated formalin-ether method (4). Serum samples were examined using the method of Single Radial Immunodiffussion (SRI) for detecting of antibodies to reveal antigen-antibody reaction with precipitation reaction. In this method specific antibody against FC part of heavy chain immunoglobulin fixed in Agar and immunoglobulins level with precipitating ring has quantitative relationship for this method we have used prepared kits of Behring Co (5).

Statistical analysis. All statistical analysis was conducted according to SPSS for Windows version 10.

Results
All 141 children (1-15 years old) were examined, 12 of them had AML (9%), and the others had ALL (91%) (Table 1). Among 129 patients with ALL, 37.2% were female (48 person) while 16.6% of patients with AML were such. The most prevalent type was L_1 (54.7%) and the least one was L_3 (6.3%). Serum analysis demonstrated normal, increased and decreased IgM titer in 58.1%, 41% and 1% of 105 examined cases respectively. As to IgG titer this value for aforementioned order was 73%, 27% and 0% in that order. In the mean time IgA titer showed normal, increase and decrease titer in 86.6%, 7.6% and 5.8% of thease cases correspondingly (Table 2). Statistical analysis showed no significant difference between the range of IgG and IgM titer and the leukemic children with intestinal parasitic infection and without infection, while IgA titer demonstrated a significant difference ($P<0.05$). Among 141 stool samples of leukemic children in 57 cases we found protozoa cyst (Table

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3). In addition, from 141 children, 53 people (21 females, and 32 males) had pathogenic and non pathogenic parasites.

he results showed that there is not any significant statistical difference among leukemic children and control group from the point of parasitic contaminations.

Table 1: Distribution of leukemic Children according to age and type of disorder

Age group	ALL	AML	Total
1 year	3	-	3
2-4	23	2	25
4-6	32	1	33
6-8	15	-	15
8-10	16	3	19
10-12	20	2	22
12-14	17	1	18
14-15	2	4	6
Total	128	13	141

Table 2: Variation of immunoglobulins in Leukemic patients comparing with control cases.

Immuno	Increase		Decrease		Normal	
globulins	*Number*	*percent*	*Number*	*percent*	*Number*	*percent*
IgM	43	41%	1	1%	61	58%
IgG	27	26%	0	0%	77	73%
IgA	8	7.6%	6	5.8%	91	86.6%
Total	78	-	7	-	229	-

Table 3: Distribution of intestinal parasites in case and control groups according to parasites species.

Name of Parasite	Case group		Control group	
	Number	*percent*	*Number*	*percent*
Giardia Lamblia	24	16.7%	8	1.04%
Blastocystis hominis	21	14.1%	4	5.7%
Entamobea histolytica	4	2.1%	2	2.8%
Entamobea coli	3	1.5%	1	1.4%
Endolimax nana	3	2.1%	1	1.4%
Iodamobea butschlii	2	2.8%	2	2.8%
Trichomonas hominis	2	2.8%	-	-
Ascaris lumbricoides	-	-	1	1.4%
Hymenolepis nana	-	-	1	1.4%
Total	* 57	-	20	-

* Two patients had more than one parasite.

Discussion

One of the most important problems in leukemia is infectious diseases. The cause of infection is disruption of normal immunity mechanisms. Normal barriers against infection are: mucosal membrane, skin, active inflammatory response of humoral and cellular Immunity. In leukemia all these barriers will be interrupted (13). The most obvious relation between infection incidence and host defense is the production and distribution of granulocytes and macrophages, which is necessary for a suitable inflammatory response (7). Granulocytes quality disorders have the most important role, but we should consider the quantity role of granulocytes more than the other (8). Defect in synthesis of specific antibody in Chronic Lymphocytic Leukemia (CLL) and multiple myeloma is the cause of increasing opsonization and body weakness in filtration of microorganisms which umoral immunity system has the main defense role against

them (9). In this research we found patients with Immunocompromised system, and ready for infections. Although as an academic discussion, there isn't any significant difference between leukemic patients and control group, (except *Blastocystis hominis* infection). In means that being Immunocompromised is not the cause of any parasitic infection. There are two reasons for absence of intestinal parasitic infection in leukemic children (10, 11).

1. Immunologic agents: Consideration of immunity process against each of these parasites and inspection of quality of injury in each of these processes in leukemic patients.

2. Pharmacologic agents: Consideration of effects of drugs on parasites in these patients, Cytotoxic drugs may posses killing effects on intestinal parasites specially worms (for their multicelluar structure) in audition to killing cancerous cells and other normal cells. Result of this research shows that in all leukemic group there is difference between recovery and life expectancy in two sexes and this is not specific for T cell-All. Recovery and life expectancy in boys are less than girls and relapse after treatment is more prevalent in boys (12). This research shows that the most sensitive age in ALL is between 2 and 6 years old. This sensitivity decreases gradually. The least rate of incidence is about 14-15 years old. This result is near to other studies that show the most incidences from 1 to 5 (9, 13). The Leukocyte count in blood peripheral smear is the most important factors in prognosis, relapse duration, recovery Period and life expectancy (14). In this study 13% of patients have leucopenia, 60% leukocytosis and 27% normal cellular count. This result shows full agreement with other studies (6). About 90% of all leukemic children had thrombocytopenia that is similar to other studies, with 92% thrombocytopenia (15). In general this research shows an increase in serum immunoglobulin during diagnosis and before treatment. In this area, two theories are considered: 1) All parts of immunity system has potential power for eradication of tumoral cells. It means that all immunity mechanisms are able to make a role in tumor control. T cells have two main ways in quarrelling with tumoral cells. B cells synthesis antibodies which have potential power for quarrelling with tumoral antigens and in control of tumor growth. 2) Increased antibodies are the result of activation of out of control done of B cells that make monoclonal antibodies. These antibodies are not able to perform their normal function. Despite of noticeable prevalence of intestinal parasites in developing countries, they are less prevalent in leukemic children. Duration of leukemia, use of cytotoxic drugs, wide use of antibiotics, duration of admition and other immunologic and pharmacologic factors, may cause to decrease prevalence of intestinal parasites in these patients.

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