THE RESULTS OF HODGKIN LYMPHOMA TREATMENT IN CHILDREN IN THE PERIOD 1997-2006

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Abstract

In this paper we present the study of chemotherapy and radiotherapy treatment success in children suffering from Hodgkin's disease (HD) that were treated at Hematology-oncology Department of Pediatric Clinic in Sarajevo.

In retrospective study we followed all patients with HD aged 0-15 who were diagnosed with and treated for HD at Pediatric Clinic in Sarajevo over the last 10 years (1st of January 1997 – 31st of December 2006).

Until 2000 we used combination of chemotherapy and radiotherapy according to UKCCSG HD 9201 treatment protocol, and after the year 2000 protocol UKCCSG HD 2000 (ChlVPP / ABVD) was applied.

The total number of the treated children 33. There were 17 boys (51,51 %) and 16 girls (48,49 %). In 10 patients (30,3 %) we found II A stage of HD, in 4 (12,1 %) II B stage of HD, in 6 children (18,8 %) stage III A, in 4 children (12,1 %) stage III B, in 4 children (12,1 %) stage IV A and in 5 (15,1 %) stage IV B. In 7 patients (21,2 %) relapse occurred, which demanded more aggressive chemotherapeutic treatment and radiotherapy too; while for 4 patients (12,1 %) in combination with bone marrow transplantation. Three patients (9,0 %) died. There are 30 children (91,0 %) who are alive and in either 1st or 2nd remission phase of HD. Secondary malignancies did not occur in any of the patients.

Although many patients (58,1%) were diagnosed in an advanced stage of illness (III and IV) the results of HD therapy at Pediatric Clinic in Sarajevo are comparable to those in other European centers.

KEY WORDS: Hodgkin's disease, diagnostics, treatment, children.

Introduction

Hodgkin's disease (Hodgkin's lymphoma) is the most frequent malignant lymphoma. It is characterized by areas of lymphoid tissue hyperplasia where Reed-Sternberg (RS) cells are located. Usually, it begins as painless lymph node enlargement, most frequently on the neck, and then disease expands to other lymph nodes and extra-lymphatic organs and infiltration of tissues may occur. Lymph nodes are larger and harder than in benign lymph node enlargement, which is usually seen in children. General symptoms like high body temperature (> 38°C), loss of body weight (> 10%) during the preceding 6 months, night sweating and skin itching are called B symptoms and are not too frequent in children. Etiology of the disease is unclear. Most probably, genetic predisposition and environmental factors are very important. Among those socioeconomic and infectious factors are of great importance. In almost 75% of cases of Hodgkin's disease in childhood it is possible to prove the involvement of Epstein-Barr virus. It is possible that there is an uncommon response to infection with Epstein-Barr virus or with some other infectious agent in combination with other factors unknown till now. Based on the diagnostic biopsy and anatomic extent the disease can be staged and treatment protocol assigned accordingly. Intra-abdominal disease is usually radiologically diagnosed by imaging techniques (Ultrasound, CT and MRI) (1, 2). Four types of Hodgkin's lymphoma can be distinguished based on patho-histological analysis: lymphocyte predomination, nodular sclerosing, mixed cellularity and lymphocyte depletion. Lymphocyte depletion is rare in children. Nodular sclerosing and mixed cellularity are found in children in almost equal ratio. Histological subtypes are in correlation with clinical picture to a certain degree. Lymphocyte predomination is more often connected with cervical and inguinal presentation while nodular sclerosis is connected with chest presentation. Success of Hodgkin's lymphoma therapy has dramatically increased over the last 40 years. With combination of chemotherapy and radiotherapy disease-free survival rate is about 80%. Fifteen years after the treatment completion it is more likely that the patient will die of complications than of HD itself. Most frequently used treatment protocols for the treatment of HD in children are: ABVD (Adriamycin, Bleomycin, Vincristine, DTIC), ChlVPP (Chlorambucil, Vinblastine, Procarbasine, Prednisone), COPP (Cyclophosphamide, Oncovin, Procarbazine, Prednisone) (3,4).

Aim of the study

The aim of this study was to estimate efficiency of chemotherapy and radiotherapy in treatment of children diagnosed with Hodgkin's disease (HD) at Haematology-oncology Department of Pediatric Clinic, University of Sarajevo Clinics Centre.

Patients and Methods

Children 0-15 years of age, suffering from HD and treated at Haematology-oncology Department of Pediatric Clinic in Sarajevo were observed in this study.
This study represents retrospective analysis of data collected from patients' histories of children suffering from HD. The data covers the period of the last ten years, from 1st January 1997 to 31st December 2006.

We analyzed:

- Patients according to sex and age
- Stage of the disease according to Ann Arbor staging system
- Patho-histological diagnoses of HD
- Type of therapy
- Outcome of HD treatment

Results

In this paper we analyzed treatment success in children diagnosed with HB at Paediatric Clinic over ten years period. In the study 33 children were observed. Sex structure and mean age of the group are presented in Table 1. We analyzed HD therapy in 17 boys and 16 girls of mean age 11.

	Total	Boys	Girls	Mean age
No	33	17	16	11 years
%	100	51,51 %	48,49 %	

TABLE 1. Patients with HD according to sex and age

Age structure of patients is presented in the Table 2. Most of our HD patients n= 14 (42,3 %) were in age group 11-15 years, and the smallest number of children n=9 (27,2 %) were in age group 0-5 years.

Age	No	%
0-5 years	9	27,2
6-10 years	10	30,3
11-15 years	14	42,4
Total	33	100%

TABLE 2. Age structure of children with HD

High percent of children were admitted in advanced stage of the disease (III and IV), the total was 58,1% (Table 3).

	Total	II A	II B	III A	III B	IV A	IV B
No	33	10	4	6	4	4	5
%	100	30,3	12,1	18,8	12,1	12,1	15,1

TABLE 3. HD according to Ann Arbor staging system

Patho-histological diagnosis was based on biopsy of an enlarged lymph node and nodular sclerosis was the most frequent finding n=14 (42%). The results of patho-histological analysis are presented in Table 4.

	Total	Nodular sclerosis	Mixed cellularity	Lymphocyte domination	Lymphocy edepletion
No	33	14	12	6	1
%	100	42,42	36,3	18,8	3,0

TABLE 4. Patho-histological diagnosis of HD

In Table 5 we present the type of therapy applied treatment of HD in our patients. Chemotherapy was performed according to United Kingdom protocol UKCCSG. All patients received chemotherapy according to the stage of their illness. 23 of them (69,7 %) received both chemo- and radiotherapy.

	Total	Chemotherapy	Chemotherapy + radiotherapy
No	33	10	23
%	100	30,3	69,7

TABLE 5. Treatment according to protocol UKCCSG HD

The outcome of our HD patients is presented on Table 6. Only 3 patients (9,0 %) died, and the rest of 30 patients (91,0 %) are alive (Table 6).

	Total	Survivals	Died
No	33	30	3
%	100	91,0	9,0

TABLE 6. Outcome of HD treatment

Discussion

According to reference data HD is somewhat more frequent in boys, which corresponds to the results of our study where we had 17 (51,51 %) boys and 16 (48,49 %) girls. Mean age of newly diagnosed in our patients was 11 years, while the youngest child was 1 year and six months old (Table 1.) It is important that HD has bimodal age distribution with first peak of incidence in early twenties and the second peak at the age of 50. In undeveloped countries the first peak occurs in early adolescence (5). HD is rarely diagnosed in patients younger than 5 years. Incidence of HD in childhood (0-15 years) is different and depends on geographic position. In Europe, incidence of HD is between 3,3 (Sweden) to 6,9 (Italy) per million inhabitants, while it is 0,6/milion in Japan (6). According to the stage of the disease (Table 3) 58,1 % children were admitted to hospital with progression of the illness (Stage III and IV), which greatly influences the outcome of the treatment. The results show that 58,33% children had « B » symptoms, which are connected with worse prognostic outcome and it was also a sign of disease progression; while 41,67 % of patients had « A » symptoms of the HD. According to patho-histological findings HD is classified into four subtypes that depend on relative ratio of H-RS cells, lymphocytes, sclerosis and fibrosis. Mixed cellular type is more frequent in younger patients in developing countries. Lymphocyte depletion is rare in children. Nodular sclerosis and mixed cell type are found in children in almost equal ratio, which corresponds to our findings (4). We found nodular sclerosis in 14 (42,42%) children, and mixed cellularity in 12 (36,3 %) children (Table 3). Children were treated according to the treatment protocol from United Kingdom UKCCSG HD (ChlVPP / ABVD) while radiotherapy of the affected regions was conducted with reduced doses of radiotherapy, adjusted to the stage of the disease and therapeutic response to chemotherapy. 10 (30,3%) children were treated with chemotherapy while 23 (69,75%) received both chemo- and radiotherapy. Therapeutic protocols for the treatment of childhood HD are multimodal (chemotherapy and radiotherapy), which enables significant decrease of doses of radiotherapy and cumulative doses of cytostatics or administration of chemotherapy only (7). Common chemotherapy scheme consists of several cycles of therapy with four agents combined. Some protocols consisted of only radiotherapy with dosage of 35 Gy for low stages of the disease, but that approach is almost entirely abandoned because of better results achieved by the combined therapy (8, 9, 10).

Conclusion

Although majority of patients (59,1%) were diagnosed in an advanced stage of the disease (III and IV) results of the HD treatment at Paediatric Clinic in Sarajevo are comparable to those in other European centres.

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