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Malignant Lymphoma in Childhood

A Retrospective Review*

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The purpose of this paper is to report a retrospective study on malignant lymphoma patients who were admitted to Hacettepe Children's Hospital over a period of years, from January 1, 1958 to December 31, 1968.

Case Material

As their biopsy specimens were available for histopathological evaluation, a total of 167 children were qualified for the study.

Age, sex, symptoms, onset of the disease, physical and laboratory findings and histological classification were studied.

76 out of 167 cases were diagnosed as Hodgkin's disease. The various clinical findings of these patients will be discussed in a separate paper. It should be mentioned here that the term "lymphosarcoma" is used with morphologic cell types of lymphoblastic, lymphocytic, mixed and giant follicular lymphomas. The term, "Leukosarcoma" is not used, since all the patients with bone marrow infiltration are accepted as having leukemia. In total, 91 patients, with lymphosarcoma and reticulum cell sarcoma, fulfilled the above criteria. 14 of these cases had reticulum cell sarcoma.

General Findings

Males composed 76.7% of all types of malignant lymphoma patients. There was an equal number of patients with Hodgkin's

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disease and lymphosarcoma (Table 1). The annual distribution of patients with various types of lymphomas is shown in Figure 1. The incidence of malignant lymphomas is shown at different ages in Figure 2. The time between the onset and histological diagnosis varied between 15 days and 36 months (Table II).

TABLE I

SEX INCIDENCE AND HISTOPATHOLOGIC TYPE OF MALIGNANT LYMPHOMA IN 167 CASES

Histologic type	Number of patients	Female %	Male %
Lymphosarcoma	77	31.1	68.9
Hodgkin's disease	76	26.3	73.9
Reticulum cell sarcoma	14	–	100
Total	167	23.3	76.7

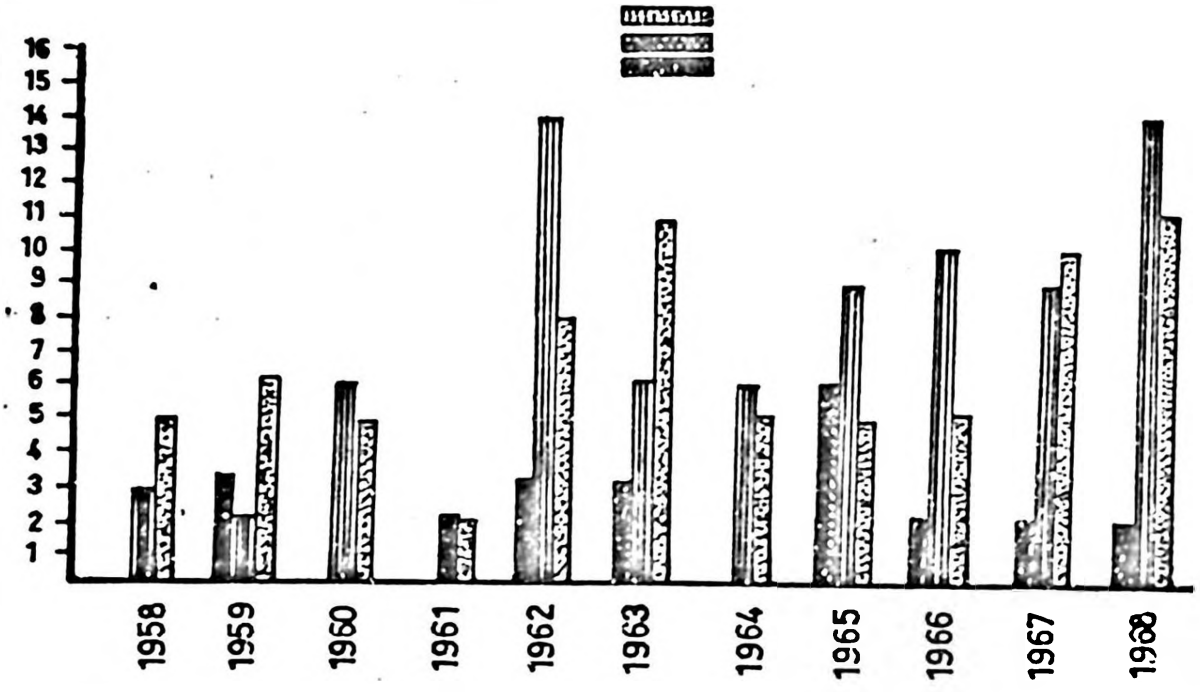

Figure 1

Findings in Patients with Lymphosarcoma :

A high percentage of the 77 children with lymphosarcoma was between the ages of 3 and 9 (Figure 2). Fifty-six out of 77 (72.7%) patients applied or were referred to our hospital with a presumptive diagnosis of a malignant disease. The remaining 21 patients were diag-

TABLE II

THE TIME BETWEEN THE ONSET OF SYMPTOMS AND HISTOLOGICAL DIAGNOSIS OF LYMPHOMA IN 91 PATIENTS

Type of Lymphoma	Time passed from the onset to the diagnosis														
	15.d*	1. m**	2. m	3. m	4. m	5. m	6. m	7. m	8. m	9. m	10. m	11. m	12. m	18. m	36. m
	***														
Lymphosarcoma	17 pt	14 pt	18 pt	13 pt	3 pt	2 pt	3 pt	–	–	2 pt	–	–	1 pt	2 pt	2 pt
Reticulum cell sarcoma	–	3 pt	4 pt	1 pt	1 pt	3 pt	1 pt	–	–	–	–	–	1 pt	–	–
Hodgkin's disease	–	2 pt	5 pt	9 pt	5 pt	3 pt	6 pt	2 pt	4 pt	3 pt	–	–	13 pt	11 pt	13 pt
Total	17 pt	19 pt	27 pt	23 pt	9 pt	8 pt	10 pt	2 pt	4 pt	5 pt	–	–	15 pt	13 pt	15 pt

* : Day
** : Month
*** : Patient

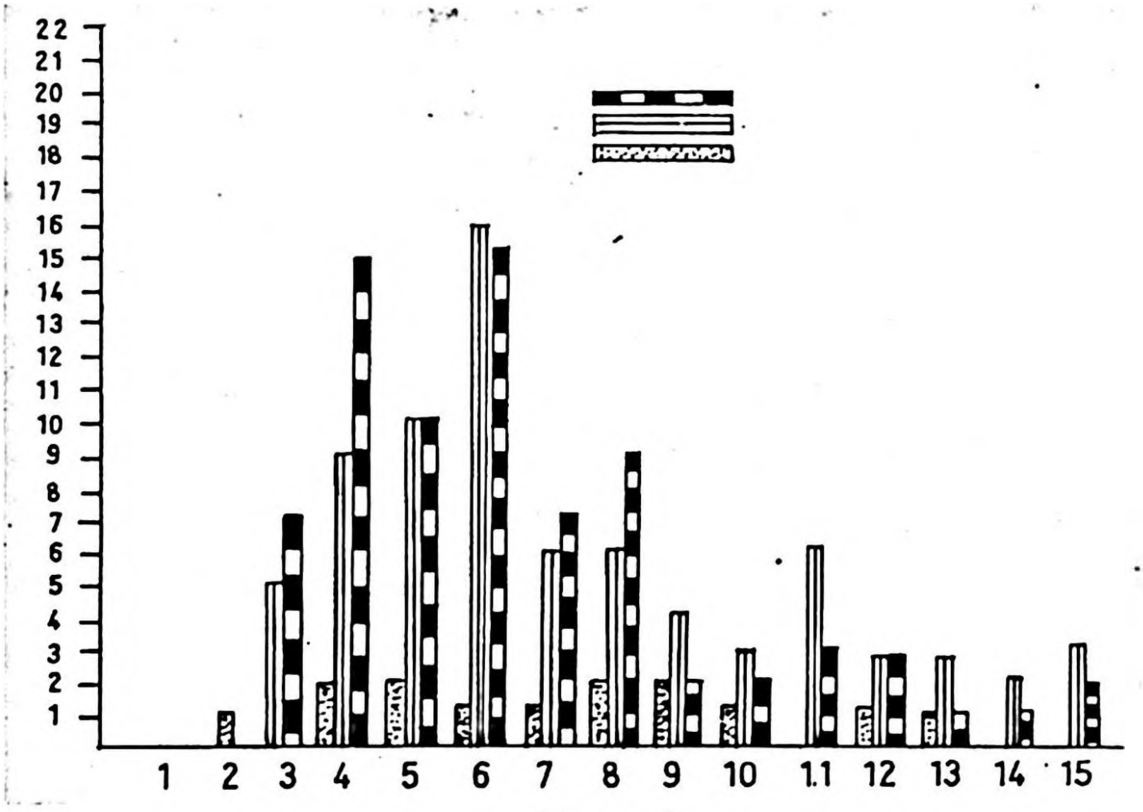

Figure 2

nosed as having various other diseases such as rheumatic fever, asthma, appendicitis, rectal prolapse, renal disease, pulmonary infection, tuberculous peritonitis, and adenitis, before entering the hospital. All these patients were seen by a physician for a period of five to eleven months before a correct diagnosis by histopathological studies was established. The major complaints of these patients successively were abdominal enlargement, abdominal pain, lumps in the neck, coughing and fever (Table III). Other complaints, not listed on the table, were loss of appetite, headache, weakness, edema, diarrhea, difficulty in swallowing, melena, dysuria and pallor.

TABLE III

COMPLAINTS OF 77 PATIENTS WITH LYMPHOSARCOMA ON THEIR ADMISSON

Complaint	Percent of the total patients
Enlargement of the abdomen	55.8
Abdominal pain	36.3
Lump in the neck	32.5
Cough	20.8
Fever	18.2
Vomiting	15.5
Shortness of breath	11.6
Weight loss	10.4

Roentgenologically, hilar lymphadenopathy was present in 20.3% of 64 chest films and pleural effusion was demonstrable in 17.2%. Deformity in the collecting system of the kidneys was found in 19.5% of 41 children. More detailed radiologic findings are shown on Table IV.

TABLE IV

RADIOLOGICAL FINDINGS OF LYMPHOSARCOMA PATIENTS

Type of study	Findings	Percent of the patients
Chest x-ray (41 cases)	1. Hilar lymphadenopathy	20.3
	2. Pleural effusion	17.2
	3. Pulmonary infiltration	7.8
I. V. P. (41 Cases)	1. Deformity of the collecting system of kidneys	19.5
	2. Displacement of kidneys	14.6
	3. Displacement of ureters	4.9
	4. Enlargement of kidneys	4.9
Barium studies of colon (17 cases)	1. Disfiguration by eyternal pressure	35.2
	2. In vagination	29.4

Erythrocyte sedimentation rate was determined in 17 children which is usually elevated (Table V). The leucocyte count varied between 10,000-20,000–per cu mm^3 and polymorphonuclear cells composed 55%-90% of all white cells on the peripheral blood smears. Groups of thrombocytes were also present on the blood films of all patients.

The hemoglobin level was found to be below 10 gm% in 26% of the patients, and its lowest level was 5 gm%. Generally the peripheral blood smears of the children with anemia showed hypochromia and microcytosis. Coombs test remained negative in all of these patients.

Four patients developed icterus during the course of the disease. Total serum bilirubin levels in these patients varied between 2-5 mg%. Serum proteins were studied in 30 patients. In 16 of these, total protein serum varied between 3.9-5.9 gm%. In five of these 14 patients serum albumin levels were below 3 gm%.

We do not have sufficient information concerning the survival time of these patients as no communication could be established in 40 out of the 77 cases. Giant follicular lymphoma was the histological diagnosis in 2 of the 5 patients whom we know to be still alive. These 2 patients

TABLE V

ERYTHROCYTE SEDIMENTATION RATE IN 17 CASES OF LYMPHOSARCOMA

Hemoglobin level (gm %	Erythrocyte sedimentation rate (m.m./hour)
5.30	25
5.75	22
6.20	48
9.37	58
10.00	19
10.28	19
10.40	32
11.50	55
11.55	42
11.55	45
11.67	31
12.65	23
14.00	14
14.00	15
15.35	56
11.95	74
13.40	42

have survived since their diseases were diagnosed seven and nine years ago. The other 3 who are still alive, were diagnosed 12, 17, and 78 months prior to this report. Out of 32 patients who died, the survival time varied between 1 day and 3 years, but the majority died within two months of the diagnosis.

Findings in reticulum cell sarcoma

There were 14 children with reticulum cell sarcoma, all of whom were male, 7 of these were referred to the hospital with the diagnosis of a tumoral disease. The other seven children were sent to our Medical Center because of the possibility of various diseases such as rheumatic fever, pulmonary infection, adenitis and stomatitis. The complaints of these children are listed on Table VI.

Intravenous pyelograms were carried out on 6 patients; enlargement of the kidneys was demonstrated on two, and displacement of the kidneys was present in the other two patients.

Roentgenograms of the skull were taken in 5 cases; in 3 of these, destructive lesions were found in mandibles.

TABLE VI

MAIN COMPLAINTS IN 14 PATIENTS WITH RETICULUM CELL SARCOMA

Complaints	Percent of the total patients
Lump in the neck	35.7
Abdominal enlargement	28.6
Abdominal pain	21.4
Loss of weight	21.4
Exophthalmus	14.2

The leucocyte count varied between 5,000 - 10,000 mm^3. Polymorphnuclear cells dominated other forms of leucocytes (55% - 70%) and groups of platelets were present on the blood smears of patients. The hemoglobin level varied between 5 - 10 gm% and Coombs test was found to be negative in all the cases.

Icterus was observed in only one reticulum cell sarcoma case in which the total bilirubin went up to 8.5 mg per cent.

Serum protein levels were determined in 8 cases and in 3 patients they were found below 6 gm%. varying between 4.6 gm% and 5.7 gm.%. In one case the serum albumin level was as low as 2.7 gm.%.

5 out of 14 patients with reticulum cell sarcoma expired in 1 day to 26 months after the diagnosis. We do not have any information about the prognosis of the other 9 patients as we could not establish any communication with these patients nor with the rest of the lymphorascoma patients.

The therapy these patients received was not uniform nor was there sufficient consistency to compare the results of various theraupeutic regimens. The biggest difficulty in the evaluation of the result of this treatment was the follow-up handicap.

Conclusion

The most common neoplasms in childhood, in order of frequency, are leukemia. central nervous system tumors and lymphomas.[1] In developed countries, from the standpoint of mortality under fifteen years of age, malignancies follow the accidents.[1]

Although in developing countries the malignancies leading to childhood mortality do not appear to be as inportant as in developed countries, the fact that we, in this hospital in the last eleven years, have

diagnosed 91 cases of malignant lymphoma, with the exclusion of Hodgkin's cases, indicates to us that we should also pay attention to this important subject. Jones and Klingberg collected 43 cases of lymphosarcoma in 15 years in a hospital of equal size to ours. These authors collected a total of 221 lymphoma cases which have been reported in a large series of literature.[2]

An analysis of 91 children with malignant lymphoma (excluding the patients with Hodkin's disease) indicated the predominance of male patients with a male–female ratio of 2.8: 1 which corresponds with the findings of others.[2,7] The male to femal predominance is more significant when the reticulum cell sarcoma cases are separately analyzed. Neither the marked male predominance nor the less frequent reticulum cell sarcoma seen in childhood were observed in adult cases.[3,4] When analysing our cases, we also took into consideration the male to female incidence and from 5,000 charts picked out at random from our outpatient population in the first 6 months of 1968, the male to female ratio was 57:43.[5]

According to this study lymphosarcoma occurs more often between the ages of 3 to 8 years. In some studies, the peak incidence of lymphomas was suggested as being between 2 and 5 years of age[6] but this is not usually the case.

As we were unable to follow up these cases, we are not in a position to comment on leukemia transformation. As mentioned previously, two of the patients with giant cell lymphoma are still alive 7 to 9 years after their diseases were diagnosed.

The time between the onset of the symptoms and the histological diagnosis is very disappointing. There were 5 cases of lymphosarcoma where a correct diagnosis was not made until 12 - 36 months after the first symptoms. However, it is not possible to definitely relate initial symptoms to the final diagnosis. It should be emphasized that there was some delay in making the correct diagnosis because these children were being treated for other obscure diagnostic possibilities such as rheumatic fever, tuberculosis etc.

Summary

A retrospective review is presented of 91 patients with malignant lymphoma (excluding Hodkin's disease). The following conclusions were drawn from the study: Malignant lymphomas is more common in boys than girls. The time from the onset of the disease to the final

histological diagnosis is unfortunately prolonged in many cases because of the lack of diagnostic facilities in a number of the hospitals, and we pediatricians should remember that lymphomas are not rare possibilities so that we may diagnose the cases much earlier.

REFERENCES

1. Miller, R. V.: Fifty-two forms of childhood cancer : United States mortality experience 1960-1966, J. Pediat. 75: 685, 1969.
2. Jones, B. and Klingberg, W. G. : Lymphosarcoma in children : A report of 43 cases and review of the recent literature, J. Pediat. 63: 11, 1963,
3. Rosenberg, S. A. et al : Lymphosarcoma in childhood, New Eng. J. Med. 259: 505, 1958.
4. Rosenberg, S. A. et al : Lymphosarcoma : The effect of therapy and survival in 1,269 patients in a review of 30 years' experience, Ann. Int. Med. 53: 877, 1960.
5. Sezer, V. : Personal communication.
6. Recent Results in Cancer Research, 1968, p. 68.
7. Bailey, R. J., Burgert, E. O. Jr. and Dahlin, D. C. : Malignant lymphoma in children, Pediatrics 28: 985, 1961.