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HODGKIN'S DISEASE IN TRUJILLO, PERU

Clinical and Histologic Presentation

PEDRO F. ALBÚJAR, MD*

A retrospective study has been made of 20 cases of Hodgkin's disease, primarily arising in lymph nodes. The cases were collected from two general hospitals of the city of Trujillo, Peru, between 1960 and 1970, and were reclassified histologically according to the Rye system. When first seen and biopsied, the majority of cases were of the histologic types associated with poor prognosis. Clinically too, most of the patients presented in advanced stages. The mortality was high. A particularly high proportion of the disease was noted in children.

THE EVOLUTION OF HODGKIN'S DISEASE IS difficult to predict purely from the histologic appearances of a biopsy, and many previous attempts to correlate histology with prognosis have led to a vast terminology of limited value. Jackson and Parker made an important advance in proposing their well-known classification. However, it has been noted that their scheme, too, is of limited prognostic value, particularly in the granulomatous type of the disease. In 1963, Lukes,[4] proposed a new system of histologic classification, based mainly on the role of the lymphocyte component of Hodgkin's infiltration; he distinguished six types and made a sharp distinction of the nodular sclerotic type. The Lukes and Butler[5] classification was accepted with minor changes, at the Rye Conference[6] in New York and is now in general use.

The observation of several fatal cases of Hodgkin's disease in the city of Trujillo, Peru, and the apparent high incidence of the disease among children led to a more detailed study on the incidence of different histologic types and their correlation with clinical presentation and subsequent evolution.

From the University of Trujillo and Belen Hospital, Trujillo, Perú.

* Associate Professor of Pathology.

Address for reprints: P. F. Albújar, MD, Universidad Nacional de Trujillo, Departamento de Medicina, Sección Patologia. Apartado No 40, Trujillo, Perú.

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MATERIALS AND METHODS

The city of Trujillo is situated on the north coast of Peru. The population was 135,865 inhabitants in 1967. For the purpose of this study, all surgical specimens diagnosed histologically as "lymphomas" were collected from the Departments of Pathology of the two general hospitals affiliated with the School of Medicine of the University of Trujillo. The period of survey was 11 years for Hospital Belen (1960 to 1970 inclusive) and seven years for Hospital Regional Docente (1964 to 1970). The great majority of patients admitted to these hospitals are mestizoes and are of low socioeconomic and nutritional levels.

After reviewing the slides, 126 cases were accepted as lymphomas. They represented 5.7% of the total of 2,200 malignant neoplasms registered in the same period; 95 cases (75%) were lymphomas primarily affecting lymph nodes and 31 (25%) arose primarily in extranodal tissues. The relative incidence of histologic types of the former group was as follows: lymphosarcoma 38 cases; reticulum cell sarcoma (histiocytic) 29 cases; Hodgkin's disease 20 cases; follicular lymphoma 4 cases; mixed type 2 cases, and unclassified 2 cases. Hodgkin's disease amounted to 21% of cases of lymphomas primarily affecting lymph nodes.

Information for clinical staging was obtained retrospectively from hospital notes. The cases were assessed according to Vera Peter's classification as recommended at the Rye Conference,[7] but because of the limited amount of information available, no attempt was made to subdivide the major goups. As lymphangiography and laparotomy had not been performed in any of the cases, there may be some underestimation of stages. A number

TABLE 1. Age and Sex Distribution in 20 Cases of Hodgkin's Disease

Age (yrs.)	No. cases	Per cent	Males	Females
0–9	4	20	3	1
10–19	4	20	3	1
20–29	3	15	3	0
30–39	2	10	2	0
40–49	1	5	1	0
50–59	1	5	0	1
60–69	2	10	1	1
70–79	3	15	2	1

of patients had received either radiotherapy or chemotherapy or both, but their possible effect on the course of the disease has not been examined in this study. It was only possible to trace 15 of 20 patients by March 1971.

Fresh histologic sections were prepared from all the biopsies of Hodgkin's disease and were stained by hematoxylin and eosin, Wilder's method for reticulum fibers, and Masson's trichrome. The cases were reclassified according to the system proposed at the Rye Conference[6] as lymphocyte predominance (LP), mixed cellularity (MC), lymphocyte depletion (LD), and nodular sclerosis (NS).

RESULTS

The age and sex distribution of patients is shown in Table 1. In the present series, the majority of patients with Hodgkin's disease have been diagnosed in the first and second decade of life. The number of cases appears to decline in the intermediate decades and increases slightly in later life; six patients were less than 15 years of age which represents 30% of the entire series. The disease was more common among males than females (sex ratio 3:1). The youngest patient was a 5-year-old boy and the oldest, a 77-year-old man.

The most common histologic types were LD (55%) and MC (30%), Table 2. There were only two examples of the LP type and a solitary case of the NS type. One of the patients of the MC group has had a second biopsy, and a change to LD pattern has been observed. The histologic types in six patients below 15 years age were: LD three cases, MC two cases, and NS one case.

TABLE 2. Histologic Types in 20 Cases of Hodgkin's Disease

	No. cases	Per cent
Lymphocyte depletion	11	55
Mixed cellularity	6	30
Lymphocyte predominance	2	10
Nodular sclerosis	1	5

TABLE 3. Histologic Types vs. Clinical Stage in 20 Cases of Hodgkin's Disease at First Presentation

Histologic types	No. cases	Clinical stage			
		I	II	III	IV
Nodular sclerosis	1	1	0	0	0
Lymphocyte predominance	2	1	0	1	0
Mixed cellularity	6	1	3	2	0
Lymphocyte depletion	11	0	1	4	6

Despite the small size of the present series, the majority of cases, when first diagnosed, were already in the more advanced stages of the disease (Table 3). On biopsy, the majority of these patients had the LD or MC types. The correlation between LD and advanced clinical stage is more striking. In the MC group, some patients presented clinically in the less advanced stages of the disease.

The eventual outcome in 15 patients in each histologic class is presented in Table 4. The two cases of LP type were still alive after 6 years and 9 years, respectively. In the MC group, two patients were alive whereas three had died within 2 years. In the LD group, only one patient was alive, although the period of observation is short; the majority of patients in this group did not survive more than one year. The one case of NS type had been lost to follow-up.

DISCUSSION

A relative high incidence of Hodgkin's disease among children in Peru has been re-

TABLE 4. Survival in Relation to Histologic Type of 15 Patients with Hodgkin's Disease

Histologic type	No. cases	Years of observation				
		1	2	3	6	9
Lymphocyte predominance	2				*	*
Mixed cellularity	5			3†	*	*
Lymphocyte depletion	8	4*	1†	2†		

* Patient alive; † patient dead.

ported by Solidoro et al.[8] In a series of 150 cases registered at the Instituto Nacional de Enfermedades Neoplasicas in Lima, 40.7% of cases were in patients below 15 years age and 30% in children below 10 years of age; the last proportion is higher than has been reported from the U.S. and most countries of Europe. (The incidence in these areas ranges from 0.5 to 8.8% in the data collected by Solidoro.[8]) Despite its brevity, the present series, which has been collected from general hospitals rather than from a specialized oncological institute, has also shown a high proportion of the disease in children, particularly male children. The apparent prevalence of the disease in this age group could be due to the high proportion of the population less than 15 years of age in Peru (estimated 45% from data collected from the Demographic Year Book of the United Nations[3]). However, detailed epidemiological studies by Correa and O'Conor[1] have shown a high age-specific incidence rate in children of Colombia, a country of similar socioeconomic development to Peru.

The histologic forms usually associated with poor prognosis (LD and MC types) were more common in this series; on the contrary, the forms of better prognosis, LP and NS, were uncommon. Correa and O'Conor[1] also found a high proportion of the types with poor prognosis in Cali, Colombia (MC 50% and LD 21.5%); they also noted a low incidence of NS type (11.7%). The findings of Chang,[2] in Lima, Peru, were different; in a series of 138 cases, the predominant type was LP (40.5%, summing up the two subtypes of his series), but the incidence of NS type was also low, 7.9%.

The epidemiological investigations of Correa and O'Conor[1] have shown at least three patterns of Hodgkin's disease. One pattern has been shown to be characterized by a bimodal age-incidence with a first peak in childhood and a second in late life: the great majority are MC or LD histologic forms. This pattern seems to prevail in developing countries. The present series of Hodgkin's disease in Trujillo conforms to this pattern, i.e., there is a high incidence of the disease in children and a tendency for the number of cases to rise again in later life. The most common forms were LD and MC, whereas the LP and NS were much more rare. In wealthy urban communities, a pattern characterized by low rates in children and NS as the prevalent histologic type has been described.

The high proportion of the more aggressive histologic types and advanced clinical stage correlate well with the high mortality that was observed in this series. This is particularly evident in the LD group in which the majority of patients died within one year. It is reasonable to assume that whatever the treatment these patients received it probably had little effect on the fatal and rapid course of the disease. The better prognosis of the LP group is confirmed with the long survival of the two cases, in spite of the fact that one of the patients was in Stage II of the disease. In the MC group, two patients were alive 3 and 4 years after diagnosis; the survival probably correlates with the less advanced clinical stage of the disease.

These observations seem to support the suggestions that the natural history of Hodgkin's disease may be affected by the interplay of environmental and host factors.[1] In this context, undernourished children with impaired immunologic competence might be expected to be more susceptible to whatever are the causal agents of Hodgkin's disease.

REFERENCES

1. Correa, P., and O'Conor, G. T.: Epidemiologic patterns of Hodgkin's disease. *Int. J. Cancer* 8:192–201, 1971.

2. Chang, A.: Enfermedad de Hodgkin: histopatologia. *Acta Cancerológica* (Lima) 6:30–41, 1967.

3. Demographic Yearbook 1970. Population trends. Statistical Office of the United Nations. Department of Economic and Social Affairs, 22nd. issue. New York 1971.

4. Lukes, R. J.: Relationship of histologic features to clinical stages in Hodgkin's disease. *Am. J. Roentgenol.* 90:944–955, 1963.

5. Lukes, R. J., and Butler, J. J.: The pathology and nomenclature of Hodgkin's disease. *Cancer Res.* 26:1063–1083, 1966.

6. Lukes, R. J., Lloyd, F. C., Hall, T. C., and Rappaport, H.: Report of the nomenclature cmmittee. *Cancer Res.* 6:1311, 1966.

7. Rosenberg, S. A.: Report of the Committee on the staging of Hodgkin's disease. *Cancer Res.* 26:1310, 1966.

8. Solidoro, A., Guzman, C., and Chang, A.: Relative increased incidence of childhood Hodgkin's disease in Peru. *Cancer Res.* 26:1204–1208, 1966.