Cancer Chemother. Pharmacol. 1, 183–186 (1978)

Cancer Chemotherapy and Pharmacology

Editorial

Chemotherapists' Need for Uniform and Rational Nomenclature and Classification of Common Lymphosarcomas and Reticulosarcoma (Hematosarcomas or Non-Hodgkin's Lymphomas)

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Chemotherapists publish the results of their protocols on hematosarcomas (lymphosarcomas and reticulosarcomas) in such a confused manner that no comparison of the different results is possible.

Firstly, they assemble several diseases under the term non-Hodgkin's lymphomas, which is inappropriate not only because of its negative designation (a definition cannot be negative), but also in that it includes diseases that are not lymphoid as far as the cells are concerned (reticulosarcoma), nor obligatorily lymphoid as far as their topographical presentation is concerned (they may be osseous or testicular, for example). This is why the term hematosarcoma is more appropriate [15].

Secondly, they use the term histiocytic [25] to define neoplasias in which the immune markers have demonstrated clearly lymphoid cells [1].

Many pathologists [2, 8, 12, 13] have proposed other nomenclatures and classifications to replace that of Rappaport, which has already been touched on [25]; Rappaport cannot be criticized for the terms he introduced since he did this at a time when we had no markers of the lymphoid cells and the several differentiation steps of these cells were not known.

However, the multiplicity of the nomenclatures and classifications proposed to replace Rappaport's do not simplify the task of chemotherapists who would like to compare their results with those of others, because the translation of any given categorization into another is very difficult, although it is not impossible (Table 1) [24].

Thus, it is important that a new categorization be adopted, integrating the WHO histocytological classification [18] and the immune marker classification [1], which both have a strong prognostic value. The integrated categorization further increases the prognostic value, distinguishing between a good-prognosis and a poor-prognosis lymphosarcoma (Fig. 1) [14, 21].

This integrated categorization of the common types recognizes:

a) The *prolymphocytic (centrofollicular) lymphosarcoma,* which is almost always a *B*-cell neoplasia (at least when centrofollicular), consists, as pointed out by Lukes et al. [13], of small or large cells with or without cleaved nuclei, the presence of which helps in the diagnosis of the diffuse form, while that of the nodular form is easy to diagnose. The term centrofollicular can only be used when the immune markers of the cells indicate that they belong to the B type, as the cells of the germinal centers are memory B cells (these centers only appear after antigenic stimulation); the first part of the word, centro- is used in order to please Lennert [12], who calls these cells centrocytes, and the second part, follicular to satisfy Bennett et al. [2], who use the term follicular cells. The term prolymphocytic is proposed because the cells of this neoplasia present a differentiation aspect between that of lymphocytes and that of blasts. It is the only safe term to use when the centrofollicular nature of the cell is not certain, because there are rare cases of T-prolymphocytic lymphosarcoma (Belpomme, unpublished data).

b) The *immunoblastic lymphosarcoma* was recognized late, after the immunoblast was described in the graft-versus-host reaction [3], identified as belonging to the lymphoid series [9], and given its name by Dameshek [6]. This type of lymphosarcoma has been recognized by Lukes [13], Lennert [12], and the WHO Reference Center for the Histological and Cytological Classification of the Neoplastic Diseases of the Hematopoietic and Lymphoid Tissues [18], and has been described as a clinical entity by our Group [17]. It can be type *T*, but is most often type *B*. Before its recognition it was included with the classic reticulosarcoma or histiocytic sarcoma [15, 25].

c) The *lymphoblastic lymphosarcoma* was described by us as early as 1963 [15]. It has been recognized by Lennert [12], and recently by Rappaport [22]. The cells resemble those of lymphoblastic acute lymphoid leukemia [16]. The common types may be *null-* or *T*-cell

0344-5704/78/0001/0183/$ 01.00

Table 1. Comparative list of terms for non-Hodgkin lymphomas [24]

WHO	Rappaport	Kiel	British Lymphoma Study Group	Lukes-Collins
1 Nodular lymphosarcoma	Malignant lymphoma, nodular	Follicular lymphoma	Follicular lymphoma	
prolymphocytic			follicle cell	follicular center cell, follicular
cleaved — small cell	lymphocytic well differentiated	centrocytic	small	cleaved — small cell
or — mixed cell	mixed lymphocytic	centroblastic-centrocytic	mixed	
non-cleaved cells — large cell	lymphocytic poorly differentiated, histiocytic	centroblastic	large	non-cleaved cells — large cell
2. Diffuse lymphosarcoma	Malignant lymphoma, diffuse	Diffuse lymphoma	Diffuse lymphoma	
(a) lymphocytic	lymphocytic, well differentiated	lymphocytic	lymphocytic, well differentiated	small lymphocyte
(b) lymphoplasmacytic	lymphocytic with plasmacytoid features	lymphoplasmacytoid (immunocytic)		plasmacytoid lymphocyte
(c) prolymphocytic				follicular center cell, diffuse
cleaved — small cell	see above	centrocytic	lymphocytic, intermediate differentiation (small follicle cell)	cleaved — small cell
or — mixed cell		centroblastic-centrocytic	mixed small lymphoid and undifferentiated large cell	
non-cleaved cells — large cell		centroblastic	undifferentiated large cell	non-cleaved cells — large cell
(d) lymphoblastic	lymphocytic poorly differentiated	lymphoblastic	lymphocytic poorly differentiated	
convoluted		convoluted		convoluted lymphocyte
non-convoluted		non-convoluted		
(e) immunoblastic	histiocytic	immunoblastic	undifferentiated large cell	immunoblastic sarcoma
(f) Burkitt's tumor	Burkitt's type	Burkitt's type	undifferentiated large cell	follicular center cell, small cell, non-cleaved
3 Reticulosarcoma	Histiocytic		True Histiocytic	Histiocytic

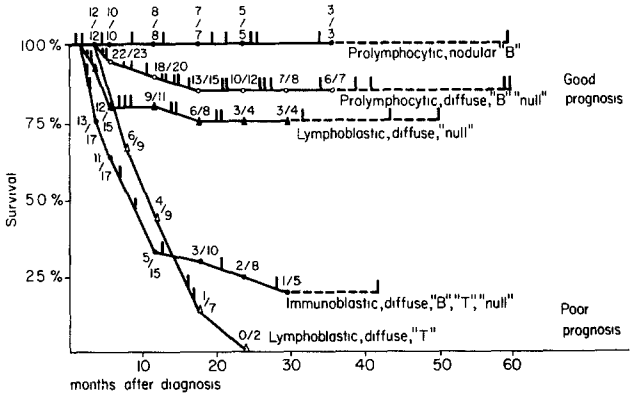

Fig. 1. Prognosis of lymphosarcomas according to the double, immune, and histocytologic WHO categorization. The population of this statistical evaluation is not exactly the same as that given in Misset's paper [21], because some of the patients included in that study were not submitted to immune-marker classification

type [1], and the T-cell type may be characterized by convoluted nuclei, as underlined by Lukes [13].

d) *Burkitt's lymphosarcoma* is a very special type of B-lymphosarcoma in Africa, where the histocytological aspect is characterized by a certain pyroninophilia of the neoplastic cells, the infiltration of the tumor by macrophages [23], and the positivity of the EBNA test [10].

Rare lymphoblastic lymphosarcomata that have *some* microscopical features of the African type but are EBNA-negative are sometimes described in other countries as Burkitt's tumors [29]. Pathologists should consider the risk they take in making such a diagnosis without immune markers. In our practice, such lymphosarcomas, if they are proven to be of the B-cell type, are called Burkitt-like, non-African lymphosarcoma.

The major aim of this integrated categorization is to make the chemotherapist foresee the prognosis, as illustrated in Figure 1, which gives the results of our experience with a chemotherapy combining adriamycin, VM 20, cyclophosphamide, and prednisone. One sees that the B-prolymphocytic centrofollicular (nodular or diffuse) type and the null-lymphoblastic type have a good prognosis under treatment with these agents. This treatment may be excessive for the nodular prolymphocytic type, in which immunotherapy alone has been shown to be active by two groups [5, 11]; alternatively this type should be treated with light rather than intensive chemotherapy [21].

In contrast, the T-lymphoblastic and both T- and B-immunoblastic types have a very poor prognosis, and further research on new chemotherapy and/or chemo-immunotherapy protocols is needed, in which new drugs such as vindesine [19] and aclacinomycine [20] must be included and in which new forms of immunotherapy

Table 2. The equivocal significance of histiocytic large-cell malignant lymphoma

	WHO nomenclature	Prognosis
Rappaport's histiocytic large-cell malignant lymphoma	Prolymphocytic large cell lymphosarcoma	Good
	Immunoblastic lymphosarcoma	Poor
	Reticulosarcoma	Intermediate

(Bach, personal communication) and thymectomy (Schlossman, personal communication) must be attempted for T types.

Unfortunately, we do not learn much from the excellent papers recently published in the literature describing remarkable results with new combinations of old drugs [4, 7] in so called large-cell histiocytic lymphomas.

This group of diseases includes, as seen in Table 2, the good-prognosis large-cell prolymphocytic (centrofollicular) diffuse lymphosarcoma and the poor-prognosis immunoblastic lymphosarcoma. Both these diseases are lymphoid in origin and not histiocytic. The intermediate-prognosis reticulosarcoma often called histocytic sarcoma, which might be a tumor of dendritic cells [26–28], and not of histiocytes, also belongs to this group. The different results of various teams may be due merely to distribution of the patients among these three WHO groups in the different trials. Hence the term histiocytic is not only a stumbling block for therapeutic progress in lymphosarcomas and reticulosarcoma, but it is also unethical, because it forces chemotherapists who have to administer intensive forms of chemotherapy for the very poor-prognosis immunoblastic lymphosarcoma to apply intensive chemotherapy also to the intermediate-prognosis reticulosarcoma and the good-prognosis prolymphocytic (centrofollicular) large-cell lymphosarcoma.

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Received July 13, 1978