History of Lymphoma Classification

1.1 Introduction

Before 1970, several purely morphologically oriented description classifications of non-Hodgkin’s lymphoma (NHL) were suggested. From that period new classifications based on current immunological concepts [Lukes-Collins classification (Lukes and Collins 1974a,b; Lukes et al. 1978b), Kiel classification (Gérard-Marchant et al. 1974; Lennert et al. 1975; Lennert 1976, 1978)] were proposed. The classification of Dorfman (1974) was a variant of the Rappaport classification. The latter was proposed by Rappaport in 1956 (Mathé et al. 1956), finalized in the Armed Forces Institute of Pathology (AFIP) fascicle “Tumors of the Hematopoietic System” in 1966 (Rappaport 1966), and then revised in 1976 (Nathwani et al. 1976). The classification of the British National Lymphoma Investigation (Bennett et al. 1974), the WHO classification (Mathé et al. 1976), and the classification of the Japanese Lymphoma Study Group (Suchi et al. 1979; see The T- and B-Cell Malignancy Study Group 1981) were independently proposed at about the same time.

In fact, in the United States a dispute developed on the widely used Rappaport classification versus the new immunologically oriented classifications (Kiel and Lukes and Collins Classification). Whereas it was almost impossible to translate from the Rappaport classification into the Kiel classification and vice versa (Krüger et al. 1981), it was relatively easy to translate back and forth between the Lukes-Collins classification and the Kiel classification (Lennert et al. 1983). The Rappaport classification was simple to use and had proved to be prognostically relevant in numerous clinical studies in the 1960s. The difference between nodular and diffuse lymphomas was particularly emphasized. It soon became clear, however, that the Rappaport classification was not consistent with the results of modern immunology, i.e., with new concepts of the lymphoid system. Nevertheless, clinical oncologists and other specialists in the United States insisted on further use of the Rappaport classification because of its simplicity and clinical relevance (clinical studies using the Lukes-Collins or the Kiel classification had not yet been done or were incomplete).

This did not solve the problem, however. Five other classifications had been proposed and were also defended emphatically by their proponents. A compromise agreement was not attained at the meeting at Airlie House in Warrenton, Virginia, USA (in 1975). In view of this situation, a large-scale study was designed, organized, and supported financially by the National Cancer Institute (NCI) of the United States that would permit all authors of the new classifications of NHL, as well as selected pathologists who were not committed to any particular classification, to review in a relatively short time a large number of previously untreated cases at different institutions. The clinical data on 1,153 cases and all histopathological diagnoses according to the six available classifications were recorded at a central facility and subsequently collated for evaluation and discussion. The end result was the presentation of a “Working Formulation of Non-Hodgkin’s Lymphoma for Clinical Usage” on January 11, 1980 in Palo Alto, California, USA (The Non-Hodgkin’s Lymphoma Classification Project 1982).

The Working Formulation (WF) was not a new classification of malignant lymphomas (MLs), but rather a terminological compromise for the definition of entities with different natural histories, prognoses, and responses to therapy. The WF clearly incorporated concepts and terms that derived from the classifications proposed by Lukes and Collins, Dorfman, and the British National Lymphoma Investigation and, to a cer-
tain extent, the Rappaport classification. In the WF, the three terms “low grade”, “intermediate grade”, and “high grade” are defined clinically, and not morphologically, which was justly pointed out by Musshoff (1987). The WF includes ten different categories within the three grades. The Kiel classification recognizes the two groups, low- and high-grade malignant lymphoma, adhering a morphological principle (which leads, nonetheless, to similar prognostic consequences). The low-grade malignant neoplasms are made up essentially of “-cytes” with, in some instances, a minority population of “-blasts”, whereas the high-grade malignant neoplasms consist mostly, or exclusively of, “-blasts”. The classification is based on morphology, and not on the results of clinical treatment. It defines biological entities.

1.2 The Kiel Classification

The old, simple classification (Lennert 1967, 1969), used in Germany until the introduction of the Kiel classification, differed from the classification recommended by Rappaport (1966), which was widely accepted in Western countries because of its apparent clinical relevance. Since neither the old German classification nor Rappaport’s classification were compatible with the knowledge gained from modern research in immunology, it was clearly necessary to apply the results of this research to neoplasms of lymphocytes and their variants. This required taking three steps: (1) the various cell types of lymphoid tissue (and lymphoid neoplasms) had to be defined by hematological and cytochemical methods; (2) the immunological characteristics (“markers”) of the morphologically identified cells had to be determined; and (3) lymphoma cells had to be morphologically and immunologically matched with their normal counterparts. These investigations led to a new understanding of ML. By taking the criteria of general pathology and hematology and the clinical behavior of ML into consideration, it was possible to propose a new classification. The so-called Kiel classification (Gérard-Marchant et al. 1974; Lennert et al. 1975; Lennert 1976) is based on that proposition (Fig. 1.1) (Table 1.1).

Lukes and Collins (1974a, b; 1975a, b; Collins et al. 1976; Lukes et al. 1978a) followed a similar course. First, they used the shape of the nuclei to characterize lymphoid cells. They distinguished follicular center cells (FCC) with cleaved nuclei from those with non-cleaved nuclei, and lymphoid cells with convoluted nuclei. At the same time, their diagnostic labels indicated whether a lymphoma is composed of B cells, T cells, or “undefined” cells. In contrast, the main terms used in the Kiel classification were originally morphological ones; “B” and “T” were found only in the names

Fig. 1.1. Karl Lennert in Kiel, in 1974, standing in front of a blackboard with the first version of the Kiel classification