Classification of the Acute Leukaemias

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ABSTRACT. A working numerical notation has been devised for the cytomorphological classification of 238 cases of acute leukaemia in adults (20 years and above) admitted by the referring centres in the United Kingdom to the Medical Research Council’s fourth and fifth therapeutic trials in acute myeloid leukaemia. Patients of 20 years and above diagnosed at the referring centres as suffering from undifferentiated leukaemia were also admitted to the trials. The diagnosis was based on May-Grünwald-Giemsa stained films of bone marrow and peripheral blood. It is intended to correlate statistically the cytomorphological subtypes with the clinical and haematological features recorded at presentation, with the remission frequency and duration, and with the duration of survival.

The notation is flexible and allows for the recognition and easy retrieval of small subgroups not accounted for by conventional nomenclature. The main subtypes are given numbers (MO to M6) and small subgroups are denoted by letters: thus, granulocytic leukaemia showing early but almost exclusively eosinophilic differentiation is designated M2E.

KEY WORDS: Morphological classification — Acute myeloid leukaemia

CLASSIFICATION OF THE ACUTE MYELOID LEUKAEMIAS

It is customary to subdivide acute myeloid leukaemia into several cytomorphological variants, but the significance of these variants in relation to other features of the disease, particularly the clinical presentation, the course of the disease, the response to treatment, and the prognosis, has not been established. The variants are recognized and named according to the main trends of cellular differentiation represented in the populations of leukaemic cells in the bone marrow and in the peripheral blood; most workers recognize five variants, namely myeloblastic, promyelocytic, myelomonocytic, monocytic and erythroleukaemic. When the blast cells in Romanowsky-stained films lack any morphological characteristics indicating differentiation, the term “undifferentiated” is used. In some of these cases cytochemical methods and electron microscopy permit the recognition of differentiation not apparent in Romanowsky-stained films. At present no reliable methods permit the distinction between some cases of undifferentiated leukaemia and lymphoblastic leukaemia, and the application is only just beginning of recently developed immunological techniques for identifying cell surface components thought to be confined to lymphocytes.

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The allocation of a particular case to one of the named variants depends on an assessment of the frequency in the leukaemic-cell population of cells showing differentiation in one or more directions. The process of identifying the leukaemic population is, however, often difficult because in undifferentiated leukaemia it is not always possible to say whether a minority of immature and mature cells of the granulocytic or erythropoietic series belongs to the residual normal haemopoietic tissue or is derived by differentiation from the leukaemic tissue. Inspection of both the bone marrow and the peripheral blood is essential, because evidence of differentiation, lacking in the bone marrow, may be obtained from the peripheral blood. Even then it may not be possible to identify the differentiated cells as normal or leukaemic.

When we began our cytomorphological survey of the cases entered into the M.R.C. fourth and fifth acute myeloid leukaemia trials, we were struck by the seemingly infinite gradation of appearances among the classical variants. Every case had been designated as acute myeloid leukaemia by the haematologist at the referring centre, and undifferentiated cell leukaemias in patients over 20 years were included in the trials (it was admitted that some of these cases might be lymphoblastic). The range of cases extended from these to well-differentiated cases that some observers might classify as “atypical chronic granulocytic leukaemia” or “chronic myelomonocytic leukaemia”. However, we did our work in ignorance of the clinical and haematological features.

May-Grünwald-Giemsa stained films were available to us in every case, and Sudan-Black and PAS preparations in most. Our diagnoses were made from the MGG films: the cytochemistry preparations often confirmed the diagnosis but we have not so far had to revise a diagnosis after examining the cytochemistry preparations.

Undifferentiated Leukaemia (M0)

In the course of our work, we came to feel that the named variants did not adequately describe the recurring patterns of differentiation of varying degree that we were observing. Moreover, we came to question the validity of the traditional practice of designating as myeloblastic an essentially undifferentiated population of blast cells amongst which, after prolonged search, a few cells could be found containing azurophilic granules, peroxidase positive granules, or Sudan Black B positivity. Do these few cells really indicate that the entire blast-cell population has originated from a clone already committed to granulocytic differentiation, but in which evidence of differentiation is confined to a tiny minority of cells, or is the cell population essentially uncommitted, with a tiny minority having undergone differentiation? We came to favour the latter view because the assumption of differentiation in a minority of cells fitted the observation, whereas the assumption of a commitment to granulocytic differentiation in the majority of undifferentiated cells seemed unwarranted. We have labelled such cases undifferentiated (M0).

If the majority of blast cells in the population are indeed uncommitted, it would be reasonable to expect that evidence of differentiation along more than one line might occasionally occur. We do not doubt that differentiation towards