

Morphological Classification of Acute Leukaemia

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Virchow (1846) was probably the first to classify leukaemias. He distinguished splenic and lymphatic forms of leukaemia on the basis of pathological distribution of tumour. During the late 1800's and early 1900's attempts were made to classify acute leukaemia's, but they were primarily exercises in taxonomy because there was no effective therapy for the disease. By 1930's nearly all morphologic forms of acute leukaemia were recognised and classifications proposed (Forkner, 1938). First successful attempts to treat acute leukaemia with chemotherapy in 1948 indicated the importance of a clinically valid classification (Farber et al., 1948). Several years after this discovery it was unclear whether the capacity for induced remissions in acute leukaemia was associated primarily with age or with type of leukaemia. However with years it was found that most of the remission obtained were in children and most children had type of leukaemia described as lymphoblastic. In early 1950's after the first trial of mercaptopurine, the importance of morphologic diagnosis was again emphasized, since it was the first drug found to have any worthwhile effect in acute myeloid leukaemia (Burchenal et al., 1953). Since then lymphoblastic and myeloblastic leukaemia have been accepted as biologically distinct groups. However there is a wide range of morphologic variation in both lymphoblastic and myeloblastic leukaemia.

In recent years attempts have been made to define subgroups and to ascertain whether there are any correlations between the subgroups, clinical and laboratory findings, response to treatment and prognosis. In addition as new, more effective chemotherapeutic drugs are put into use, many protocols are based on morphologic presentations of patients..

There is a wide range of morphologic appearances in the acute lymphoblastic and non myeloid leukaemia. Attempts to categorize the heterogeneity have been made on the basis of cell size and degree of immaturity. The French American-British co-workers in their first formal classification of leukaemias, found that with most patients having lymphoblastic, morphologic characteristics of the blast cells were homogenous enough to suggest a natural group. A rare but very homogenous group with a monomorphic cell population resembling that of the Burkitt type lymphoma also was a readily separated natural group. A substantial minority remained mostly adult patients with considerable morphologic variation between one another, but also characterised by the marked heterogeneity in the cell population in any one patient. Thus three broad divisions of undifferentiated non-myeloid blast cell leukaemia emerged. Because the majority fell into the first group of childhood leukaemia, traditionally called lymphoblastic, the term was retained for the whole group (Bennett et al, 1976; FAB classification). The three categories of lymphoblastic leukaemia are designated, L 1 homogenous population of blasts with high nuclear cytoplasmic ratio and absent or small nucleoli. L 2 : Heterogenous population of blasts with low nuclear cytoplasmic ratio and prominent nucleoli. L 3 : homogenous group with cytomorphology of Burkitt lymphoma with all cells having vacuolated cytoplasm (Bennett et al., 1976; Bennett et al., 1981).

Blast cell leukaemias of myeloid origin arising from a stem cell committed for differentiation along one or more of the granulocytic, monocytic or erythrocytic pathways, have long been known to show marked morphologic variation. Certain variants have been associated with particular clinical manifestations like Monocytic and myelomonocytic leukaemia with gum hypertrophy (Forkner, 1934) and skin infiltration (Mercer, 1935) and Hypergranular promyelocytic leukaemia with intravascular coagulation (Gralnick and Sultan, 1975). Formal morphologic classification of acute myeloblastic leukaemia presents difficulties because pure variants are linked by intermediate cases. However the very existence of pure variants justifies attempts at classification. The FAB group defined three variants

of acute myeloid leukaemia showing predominantly granulocytic differentiation. M 1: Blasts showing minimal evidence of differentiation and no maturation. M 2 : Blasts showing clear evidence of maturation to the promyelocyte stage and beyond. M 3: Hypergranular promyelocytic leukemia, a special variant with highly abnormal cells packed with abnormal azurophilic granules or with numerous Auer rods. The FAB group defined two classic variants of acute myeloid leukaemia that include a monocytic component. M 5 :Pure monoblastic leukemia. It exists in two forms (a) almost all cells are blasts, (b) a high proportion of cells have matured beyond the promonocyte stage.M 4: in this form both granulocytic and monocytic components coexist in varying proportion and showing varying maturation in both granulocytic and monocytic series. Finally FAB group defined M 6: erythroleukaemia, where high proportion of all the cells in the marrow are erythroblasts and there is severe dyserythropoiesis (Bennett et al., 1976).

Morphologic classification of acute leukaemias applies only to blood and marrow samples from untreated patients and are not valid if applied to treated patients (Bennett et al., 1976). The ultimate test of this morphologic classification lies in its ability to segregate responders from non-responders in retrospective protocols or to predict response in prospective protocols.

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