FAB CLASSIFICATION OF ACUTE LEUKAEMIA

Pages with reference to book, From 28 To 29

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In 1857 Virchow[1] was probably the first to classify leukaemia. He distinguished splenic and lymphatic forms of leukaemia. Although attempts to classify acute leukaemia during the late 1800's and early 1900's were scientifically sound, these classifications were primarily exercises in taxonomy because there was no effective therapy for the disease. Early 1950's saw introduction of successful chemotherapy of acute leukaemia by adrenal corticosteroid, folic acid antagonists[2] and mercaptopurine[3]. These attempts indicated the importance of a clinically valid classification. Since then the fact that "lymphoblastic" and "myeloblastic" leukaemia are biologically distinct groups has never been disputed. However, there is a wide range of morphologic variation. Therefore, attempts were made to define sub-groups and to ascertain whether there were any correlations between these sub-groups and clinical and laboratory findings, response to treatment and prognosis. In 1976[4] a group of seven French, American and British haematologists met with the aim of making proposals on nomenclature and morphologic classification of acute leukaemia that might serve as a basis from which a generally acceptable system could be worked out and of defining features of each named entity as objectively and unambiguously as possible. This classification is now generally referred to as FAB-classification. FAB-group described three variants of lymphoblastic leukaemia Li, L2 and L3. Li, a homogenous population of blasts with indistinct or small nucleoli, regular nuclear membrane outline and high nuclear cytoplasmic ratio. L2, a heterogenous population of blasts with prominant nucleoli, irregular nuclear membrane outline and low nuclear cytoplasmic ratio. L3; a homogenous population, with prominant nucleoli, basophilic cytoplasm and cytoplasmic vacuolation. FAB group described six main types of acute myeloid leukaemia Ml, M2, M3, M4, M5 and MG. These were defined according to (a) the direction of differentiation along one or more cell lines and (b) the degree of maturation of the cells. Thus Ml, M2 and M3 show predominantly granulocytic differentiation and differ from one another in the extent and nature of granulocytic maturation.M4 shows both granulocytic and monocytic differentiation, MS predominantly monocytic and M6 predominantly erythroblastic differentiation. Ml, myeloblastic leukaemia without maturation. Cells in bone marrow show some evidence of granulocytic differentiation. Blasts show one or more distinct nucleoli and upto 3% of blasts show auer rods and azurophilic granuoles. M2, myeloblastic leukaemia with maturation. Maturation beyond promyelocyte. M3, hypergranular promyelocytic leukaemia. Great majority of cells are abnormal promyelocytes with characteristic pattern of heavy granulation M4, myelomonocytic leukaemia. Both granulocytic and monocytic differentiation are present in varying proportions in bone marrow and peripheral smear M5, monocytic leukaemia. Two sub-types occur, (a) poorly differentiated characterised by large blasts in the bone marrow and peripheral blood. The blasts have delicate lacy-chromatin and one, occasionally upto three large prominent vesicular nucleoli. The cytoplasm is voluminous and often shows one or more pseudopods. Type (b) is differentiated with monoblasts, promonocytes and monocytes. Diagnosis often requires cytochemical confirmation by fioride inhibited esterase reaction MG, erythroleukaemia. The erythropoietic component usually exceeds 50% of all the nucleated cells in the bone marrow and the erythroblasts show in varying degree, bizarre morphologic features, especially multiple lobution of the nucleus, with variation in size of the lobes, multiple nuclei, giant forms and megaloblastic features. FAB group emphasized that this classification can only be applied and is valid for bone marrow and/or peripheral blood of untreated cases. FAB classification has been found useful in predicting response to therapy, relapse rates and prognosis in both adult and childhood ALL, a better prognosis of Li, as compared to 1.2[5-10]. Considering FAB classification of acute myeloid leukaemia, earlier studies

showed that there was no difference between the two major categories, acute myeloid leukaemia or acute myelomonocytic leukaemia in either response rates, duration of response or median survival[11] However, others found M4 and MS to have longer survival than Ml and M3[12,13]. Nevertheless FAB classification is now universally accepted as the first step in classification and diagnosis of leukaemia. Subsequent analysis e.g., cytochemical markers, monoclonal antibody markers and therapeutic regimens are all correlated to this classification[14,15]. In recent years acute leukaemia has been classified by this classification in Pakistan[16-19]. Others have started using this classification and this will thus provide a first step in morphologic categorisation of acute leukaemia in Pakistan.

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