What Is Burkitt’s Lymphoma and When Is It Endemic?

To the Editor:

Denis Burkitt first published an account of the tumor that bears his name in 1958. In the following years, there was considerable confusion concerning the nature of the tumor, its relationship to other lymphomas, and whether it occurred outside Africa. To clarify this matter, the World Health Organization, in collaboration with the International Agency for Research on Cancer, convened a meeting of 18 hematopathologists in Washington in October 1967. Histological and cytological preparations from 55 selected cases were circulated to the participants before the meeting. The conclusions of the majority of the participants were that “the eponym Burkitt’s tumour is best applied to a malignant neoplasm of the haemopoietic system composed of a predominant and characteristic cell type,” and that “Burkitt’s tumour, as defined above, is not limited to Africa and occurs in many parts of the world.” Two members of the group (Dr Iris Hamlin and Dr Philip Lieberman) dissented from this view. They were of the opinion that Burkitt’s lymphoma (BL) is a clinicopathological concept only and does not exist in a specific histological or cytological sense. As so often happens in the history of medicine, time has shown both groups to have truth on their side.

BL undoubtedly exists as a morphological entity identifiable in good quality histological and cytological preparations. The reasons for this are the characteristic translocations between the c-myc gene and the Ig genes that occur in all subtypes of BL and result in c-myc deregulation. Tumor cells remain permanently in cycle and do not differentiate imposing cytological uniformity on the tumor. Because all cells are in cycle, all viable tumor cells will be labeled with an appropriate proliferation marker such as Ki67, giving a labeling index of 100%. This provides useful supporting evidence for a diagnosis of BL. However, the minority group was correct in emphasizing the need for clinicopathological correlation. Within the morphological spectrum of BL, there are three subtypes: endemic BL (eBL), sporadic BL (sBL), and acquired immunodeficiency syndrome-related BL (AIDS-BL). eBL occurs almost exclusively in children, with a peak age incidence of 7 years. The predominant sites of involvement are the kidneys, liver, mesentry and retroperitoneum, gonads, and endocrine glands. Jaw tumors (usually involving multiple quadrants) are a characteristic feature, but are age dependent, and in African communities are usually found in 50% of cases. In contrast, sBL occurs in children and young adults and usually presents as lower abdominal masses frequently involving the terminal ileum or as tumors of Waldeyer’s ring. AIDS-BL occurs in young adults and frequently involves lymph nodes and bone marrow. Epstein-Barr virus (EBV) is associated with virtually 100% of cases of eBL. Only 20% to 35% of sBLs in Europe and North America are EBV positive. In South Africa and parts of the Middle East, this increases to 50% to 80%. Despite the fact that most patients with AIDS carry a large burden of EBV, only 30% of AIDS-BL are EBV positive. All types of BL have translocations involving the c-myc gene and the Ig genes. However, the breakpoints in relation to these genes differ between eBL and the other subtypes.8

Although there are undoubtedly borderline cases, the majority of eBL, sBL, and AIDS-BL form distinct clinicopathological entities. They may well differ in the cell of origin and almost certainly differ in their pathogenesis. It is unfortunate that the three subtypes were not clearly delineated in the REAL classification,9 and it is to be hoped that the WHO classification, when it appears, will rectify this deficiency. A further problem that has arisen from the recognition of only one type of BL is that eBL is often defined by geography alone. In a recent study on the cell kinetics and immunophenotype of BL, 10 cases were defined as eBL because they came from the lowlands of Kenya. Three of these cases were young human immunodeficiency virus (HIV)-positive adults, 2 had cervical lymphadenopathy, and 1 had a tumor in the terminal ileum. These cases clearly fall into the category of AIDS-BL. It is probable that sBL also occurs in Africa and may account for the rare EBV-negative cases of BL reported from that continent. In a recent paper in BLOOD11 on the molecular analysis of EBV in eBL, the specimens were defined as endemic because they were obtained through The National Cancer Institute’s BL Project at the University of Ghana. Despite the impeccable molecular studies reported in Tao et al,11 the reader cannot judge whether these are cases of eBL, a mixture of eBL and AIDS-BL, or even sBL. It is quite clear, particularly since the AIDS epidemic, that cases cannot be assumed to be eBL simply because they originate from Africa. Semantics are the bug-bear of hematopathology, but to avoid further confusion, it might be better to change the terms endemic and sporadic to endemic type and sporadic type.

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REFERENCES
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