Table 13-8 Subtypes of Hodgkin Lymphoma

Subtype	Morphology and Immunophenotype	Typical Clinical Features
Nodular sclerosis	Frequent lacunar cells and occasional diagnostic RS cells; background infiltrate composed of T lymphocytes, eosinophils, macrophages, and plasma cells; fibrous bands dividing cellular areas into nodules. RS cells CD15+, CD30+; usually EBV–	Most common subtype; usually stage I or II disease; frequent mediastinal involvement; equal occurrence in males and females (F = M), most patients young adults
Mixed cellularity	Frequent mononuclear and diagnostic RS cells; background infiltrate rich in T lymphocytes, eosinophils, macrophages, plasma cells; RS cells CD15+, CD30+; 70% EBV+	More than 50% present as stage III or IV disease; M greater than F; biphasic incidence, peaking in young adults and again in adults older than 55
Lymphocyte rich	Frequent mononuclear and diagnostic RS cells; background infiltrate rich in T lymphocytes; RS cells CD15+, CD30+; 40% EBV–	Uncommon; M greater than F; tends to be seen in older adults
Lymphocyte depletion	Reticular variant: Frequent diagnostic RS cells and variants and a paucity of background reactive cells; RS cells CD15+, CD30+; most EBV+	Uncommon; more common in older males, HIV-infected individuals, and in developing countries; often presents with advanced disease
Lymphocyte predominance	Frequent L&H (popcorn cell) variants in a background of follicular dendritic cells and reactive B cells; RS cells CD20+, CD15–, C30–; EB–	Uncommon; young males with cervical or axillary lymphadenopathy; mediastinal

L&H, lymphohistiocytic; RS cell, Reed-Sternberg cell.

advanced tumor stage. Nonetheless, the overall prognosis is very good.

Lymphocyte-Rich Type. This is an uncommon form of classical HL in which **reactive lymphocytes make up the vast majority of the cellular infiltrate**. In most cases, involved lymph nodes are diffusely effaced, but vague nodularity due to the presence of residual B-cell follicles is sometimes seen. This entity is distinguished from the lymphocyte predominance type by the presence of frequent mononuclear variants and diagnostic Reed-Sternberg cells with a "classical" immunophenotypic profile. It is associated with EBV in about 40% of cases and has a very good to excellent prognosis.

Lymphocyte Depletion Type. This is the least common form of HL, amounting to less than 5% of cases. It is characterized by a paucity of lymphocytes and a relative abundance of Reed-Sternberg cells or their pleomorphic variants. The immunophenotype of the Reed-Sternberg cells is identical to that seen in other classical types of HL. Immunophenotyping is essential, since most tumors suspected of being lymphocyte depletion HL actually prove to be large-cell NHLs. **The Reed-Sternberg cells are infected with EBV in over 90% of cases.**

Lymphocyte depletion HL occurs predominantly in older adults, in HIV+ individuals of any age, and in nonindustrialized countries. Advanced stage and systemic symptoms are frequent, and the overall outcome is somewhat less favorable than in the other subtypes.

Lymphocyte Predominance Type. This uncommon "nonclassical" variant of HL accounts for about 5% of cases. Involved nodes are effaced by a nodular infiltrate of small lymphocytes admixed with variable numbers of macrophages (Fig. 13-27). "Classical" Reed-Sternberg cells are usually difficult to find. Instead, this tumor contains so-called L&H (lymphocytic and histiocytic) variants, which have a multilobed nucleus resembling a popcorn kernel ("popcorn cell"). Eosinophils and plasma cells are usually scant or absent.

In contrast to the Reed-Sternberg cells found in classical forms of HL, **L&H variants express B-cell markers typical of germinal-center B cells**, such as CD20 and BCL6, and are usually negative for CD15 and CD30. The typical nodular pattern of growth is due to the presence of expanded B-cell follicles, which are populated with L&H variants, numerous reactive B cells, and follicular dendritic cells. The IgH genes of

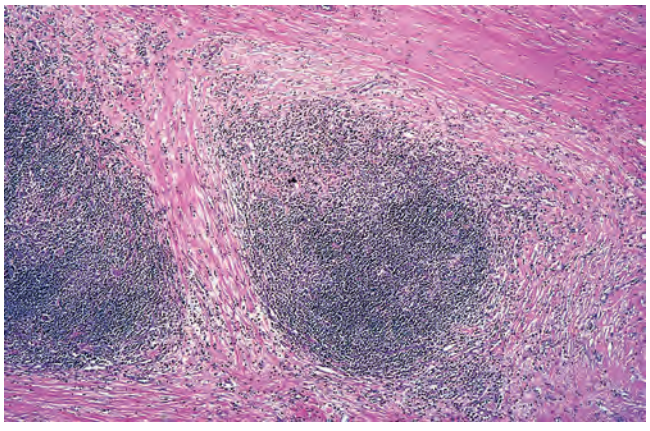

Figure 13-25 Hodgkin lymphoma, nodular sclerosis type. A low-power view shows well-defined bands of pink, acellular collagen that subdivide the tumor into nodules. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex.)

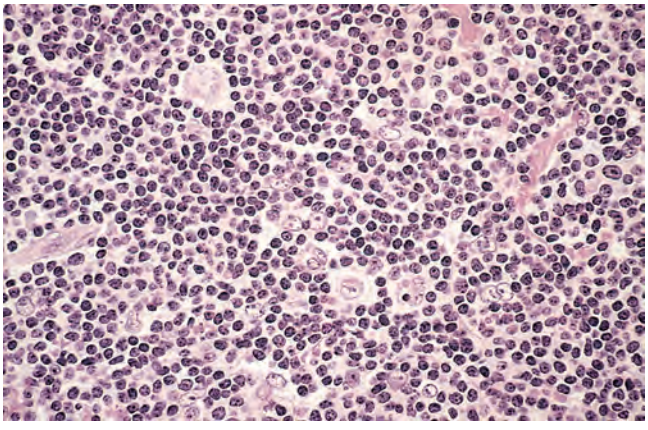

Figure 13-26 Hodgkin lymphoma, mixed-cellularity type. A diagnostic, binucleate Reed-Sternberg cell is surrounded by reactive cells, including eosinophils (bright red cytoplasm), lymphocytes, and histiocytes. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Tex.)