malignancy. In this simple system there are only three histologic subtypes:

- Tumors that are cytologically benign and noninvasive
- Tumors that are cytologically benign but invasive or metastatic
- Tumors that are cytologically malignant (thymic carcinoma)

In all categories, the tumors usually occur in adults older than 40 years of age; thymomas are rare in children. Males and females are affected equally. Most arise in the anterior superior mediastinum, but sometimes they occur in the neck, thyroid, pulmonary hilus, or elsewhere. They are uncommon in the posterior mediastinum. Thymomas account for 20% to 30% of tumors in the anterosuperior mediastinum, which is also a common location for certain lymphomas.

MORPHOLOGY

Macroscopically, thymomas are lobulated, firm, gray-white masses of up to 15 to 20 cm in size. They sometimes have areas of cystic necrosis and calcification. Most are encapsulated, but 20% to 25% of the tumors penetrate the capsule and infiltrate perithymic tissues and structures.

Noninvasive thymomas are most often composed of medullary-type epithelial cells or a mixture of medullary and cortical type epithelial cells. The medullary type epithelial cells are elongated or spindle-shaped (Fig. 13-41*A*). There is usually a sparse infiltrate of thymocytes, which often recapitulate the phenotype of medullary thymocytes. In mixed thymomas there is an admixture of polygonal cortical type epithelial cells and a denser infiltrate of thymocytes. The medullary and mixed patterns together account for about 50% of all thymomas. Tumors that have a substantial proportion of medullary-type epithelial cells are usually noninvasive.

Invasive thymoma refers to a tumor that is cytologically benign but locally invasive. These tumors are much more likely to metastasize. The epithelial cells are most commonly of the cortical variety, with abundant cytoplasm and rounded vesicular nuclei (Fig. 13-41*B*), and are usually mixed with numerous thymocytes. In some cases, the neoplastic cells show cytologic atypia, a feature that correlates with a propensity for more aggressive behavior. These tumors account for about 20% to 25% of all thymomas. **By definition, invasive thymomas penetrate through the capsule into surrounding structures.** The extent of invasion has been subdivided into various stages, which are beyond our scope. With minimal invasion, complete excision yields a 5-year survival rate of greater than 90%, whereas extensive invasion is associated with a 5-year survival rate of less than 50%.

Thymic carcinoma represents about 5% of thymomas. Macroscopically, they are usually fleshy, obviously invasive masses, sometimes accompanied by metastases to sites such as the lungs. Microscopically, most are **squamous cell carcinomas**. The next most common variant is **lymphoepithelioma-like carcinoma**, a tumor composed of sheets of cells with indistinct borders that bears a close histologic resemblance to nasopharyngeal carcinoma. About 50% of lymphoepithelioma-like carcinomas contain monoclonal EBV genomes, consistent with a role for EBV in their pathogenesis. A variety of other less common histologic patterns of thymic carcinoma have been described; all exhibit cytologic atypia seen in other carcinomas.

Clinical Features. About 40% of thymomas present with symptoms stemming from impingement on mediastinal structures. Another 30% to 45% are detected in the course of evaluating patients with myasthenia gravis. The rest are discovered incidentally during imaging studies or cardiothoracic surgery. In addition to myasthenia gravis, other associated autoimmune disorders include hypogammaglobulinemia, pure red cell aplasia, Graves disease, pernicious anemia, dermatomyositis-polymyositis, and Cushing syndrome. The basis for these associations is still obscure, but the thymocytes that arise within thymomas give rise to long-lived CD4+ and CD8+ T cells, and cortical thymomas rich in thymocytes are more likely to be associated with autoimmune disease. Hence, it seems likely that abnormalities in the selection or "education" of T cells maturing within the environment of the neoplasm contribute to the development of diverse autoimmune disorders.

SUGGESTED READINGS

Hematopoietic Stem Cells

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