seminomas, all of which are of uncertain origin. ITGCN is believed to arise in utero and stay dormant until puberty, after which it may progress to seminoma or nonseminomatous tumors. The lesion consists of atypical primordial germ cells with large nuclei and clear cytoplasm, which are about twice the size of normal germ cells. These cells retain the expression of the transcription factors OCT3/4 and NANOG, which are important in maintenance of pluripotent stem cells. ITGCN shares some of the genetic alterations that are found in germ cell tumors. One that is particularly important is the reduplication of the short arm of chromosome 12 (12p) in the form of an isochromosome i(12p), a cytogenetic alteration that is invariably found in invasive germ cell tumors regardless of histological type. Activating mutations in the gene encoding the KIT receptor tyrosine kinase, which may be present in seminomas, are also freqeuntly present in ITGCN. About 50% of individuals with ITGCN develop invasive germ cell tumors within five years after diagnosis, and it may be that practically all patients with ITGCN will eventually develop invasive tumors.

Seminoma

Seminomas are the most common type of germ cell tumor, making up about 50% of these tumors. The peak incidence is the third decade and they almost never occur in infants. An identical tumor arises in the ovary, where it is called *dysgerminoma* (Chapter 22). Seminomas contain isochromosome 12p and express OCT3/4 and NANOG. Approximately 25% of these tumors have *KIT* activating mutations. *KIT* amplification and *KIT* overexpression through other unknown mechanisms have also been reported.

MORPHOLOGY

If not otherwise specified, "seminoma" refers to "classic" or "typical" seminoma. Spermatocytic seminoma, despite its similar name, is a distinct tumor discussed later. Seminomas produce bulky masses, sometimes ten times the size of the normal testis. The typical seminoma has a homogeneous, gray-white, lobulated cut surface, usually devoid of hemorrhage or necrosis (Fig. 21-23). Generally the tunica albuginea is not penetrated, but occasionally extension to the epididymis, spermatic cord, or scrotal sac occurs.

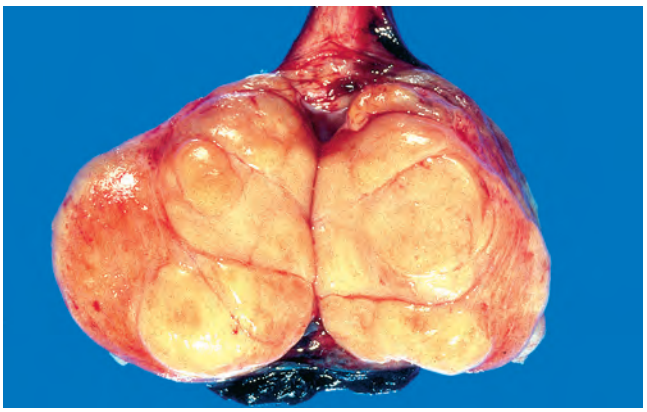

Figure 21-23 Seminoma of the testis appears as a fairly well-circumscribed, pale, fleshy, homogeneous mass.

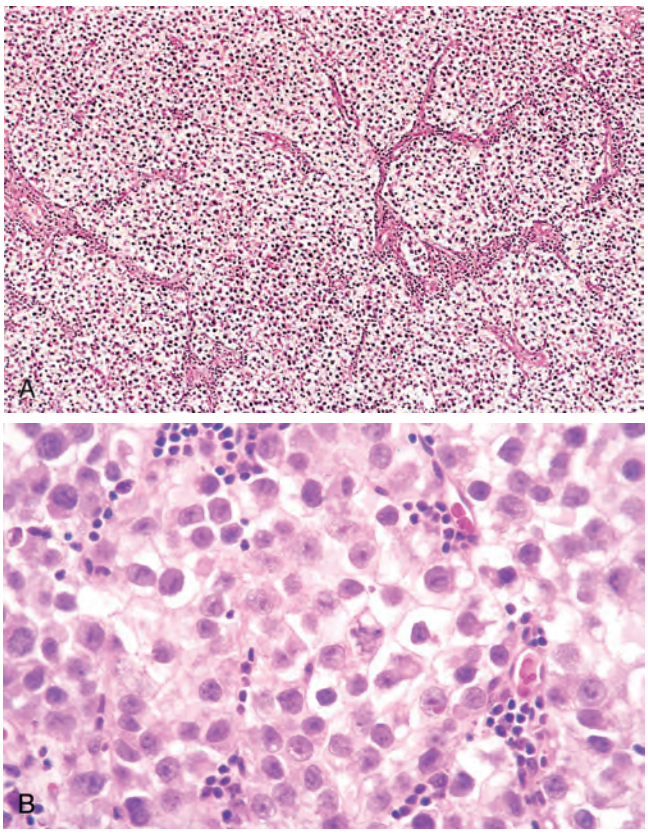

Figure 21-24 Seminoma. **A,** Low magnification shows clear seminoma cells divided into poorly demarcated lobules by delicate septa. **B,** Microscopic examination reveals large cells with distinct cell borders, pale nuclei, prominent nucleoli, and a sparse lymphocytic infiltrate.

Microscopically the typical seminoma is composed of sheets of uniform cells divided into poorly demarcated lobules by delicate fibrous septa containing a lymphocytic infiltrate (Fig. 21-24*A*). **The classic seminoma cell is large and round to polyhedral and has a distinct cell membrane; clear or watery-appearing cytoplasm; and a large, central nucleus with one or two prominent nucleoli** (Fig. 21-24*B*). Mitoses vary in frequency. The cytoplasm contains varying amounts of glycogen. Some tumors have anaplastic features (anaplastic seminoma), including frequent tumor giant cells and greater mitotic activity, but this does not appear to portend a worse prognosis when matched for stage with classic seminoma. By immunohistochemistry, seminoma cells stain positively for KIT, (regardless of KIT mutational status), OCT4, and placental alkaline phosphatase (PLAP). A few scattered keratin-positive cells may also be present.

Approximately 15% of seminomas contain syncytiotrophoblasts. In this subset of patients, serum human chorionic gonadotropin (HCG) levels are elevated, though not to the extent seen in patients with choriocarcinoma. Seminomas may also be accompanied by an ill-defined granulomatous reaction, in contrast to the well-formed discrete granulomas seen with tuberculosis.

Spermatocytic Seminoma

In contrast to the classic seminoma described earlier, spermatocytic seminoma is a rare, slow-growing germ cell