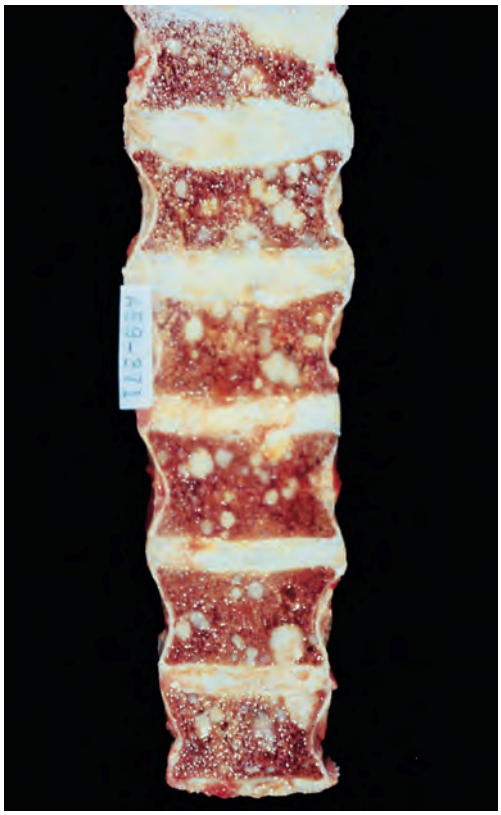

Figure 21-35 Metastatic osteoblastic prostatic carcinoma within vertebral bodies.

nodes. Hematogenous spread occurs chiefly to the bones, particularly the axial skeleton, but some lesions spread widely to viscera. Massive visceral dissemination is an exception rather than the rule. The bony metastases are typically osteoblastic, a feature that in men points strongly to a prostatic origin (Fig. 21-35). The bones commonly involved, in descending order of frequency, are lumbar spine, proximal femur, pelvis, thoracic spine, and ribs.

Histologically, most lesions are adenocarcinomas that produce well-defined, readily demonstrable gland patterns. The glands are typically smaller than benign glands and are lined by a single uniform layer of cuboidal or low columnar epithelium. In contrast to benign glands, prostate cancer glands are more crowded, and characteristically lack branching and papillary infolding. **The outer basal cell layer typical of benign glands is absent.** The cytoplasm of the tumor cells ranges from pale-clear to a distinctive amphophilic appearance. Nuclei are large and often contain one or more large nucleoli. There is some variation in nuclear size and shape, but in general pleomorphism is not marked. Mitotic figures are uncommon.

The diagnosis of prostate cancer on biopsy specimens can be challenging due to several factors. There is often only a scant amount of tissue available for histologic examination in needle biopsies, and malignant glands may be admixed with numerous benign glands (Fig. 21-36). Moreover, the histologic findings pointing to malignancy may be subtle (leading to underdiagnosis), and there are also benign mimickers of cancer that can lead to a misdiagnosis of cancer. A few histologic findings on biopsy are specific for prostate cancer, such as perineural invasion, but in general the diagnosis is made based on a constellation of architectural, cytologic, and ancillary findings (Fig. 21-37). As discussed earlier, one distinguishing feature between benign and malignant prostate glands is that benign glands contain basal cells, which are absent in cancer (compare benign and malignant glands in Fig. 21-36*A*, and benign glands in Fig. 21-33*C* with cancerous glands in Fig. 21-36*B*). This distinction can be brought out by using various immunohistologic markers to label basal cells. Another useful immunohistochemical marker is α-methylacyl-coenzyme A-racemase (AMACR), which is up-regulated in prostate cancer. The majority of prostate cancers are positive for AMACR, the sensitivity varying among studies from 82% to 100%. Such markers, while improving diagnostic accuracy, are still prone to false-positive and false-negative results and must be used in conjunction with the routine hematoxylin and eosin–stained sections.

In approximately 80% of cases, prostatic tissue removed for carcinoma also harbors presumptive precursor lesions, referred to as **high-grade prostatic intraepithelial neoplasia (PIN)**. PIN consists of architecturally benign large, branching prostatic acini lined by cytologically atypical cells with prominent nucleoli. Cytologically PIN and carcinoma may be identical. Unlike malignant glands, PIN glands are surrounded by a patchy layer of basal cells and an intact basement membrane.

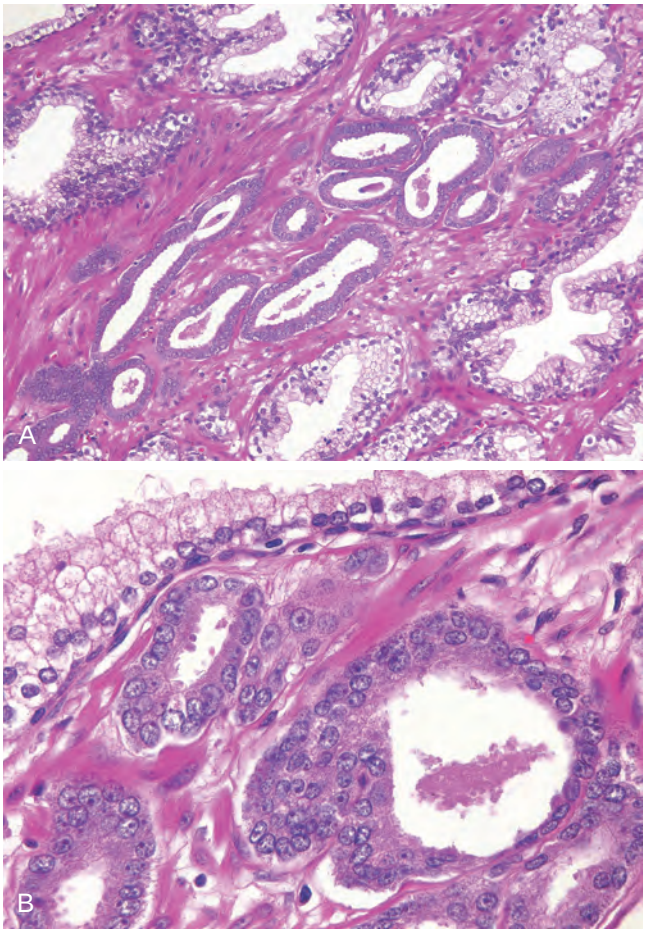

Figure 21-36 **A,** Photomicrograph of small focus of adenocarcinoma of the prostate demonstrating small glands crowded in between larger benign glands. **B,** Higher magnification shows several small malignant glands with enlarged nuclei, prominent nucleoli, and dark cytoplasm, compared with larger benign gland *(top)*.