



Figure 23-23 Grading of invasive carcinoma. **A**, A well-differentiated carcinoma of no special type consists of tubules or a cribriform pattern of cells with small monomorphic nuclei. **B**, A moderately differentiated carcinoma of no special type shows less tubule formation and more solid nests of cells and pleomorphic nuclei. **C**, A poorly differentiated carcinoma of no special type infiltrates as ragged sheets of pleomorphic cells and contains numerous mitotic figures and central areas of tumor necrosis.

imperceptible (Fig. 23-22G, H), being comprised of scattered neoplastic glands or single tumor cells infiltrating otherwise unremarkable fibrofatty tissue (Fig. 23-22).

Larger carcinomas may invade the pectoralis muscle and be fixed to the chest wall or invade into the dermis and cause dimpling of the skin. When the tumor involves the central portion of the breast, retraction of the nipple may develop. Rarely, breast cancer presents as metastasis to an axillary node or distant metastasis before cancer is detected in the breast. In such cases, the primary carcinoma may be small, or be obscured by dense breast tissue, or fail to produce a desmoplastic response, making it difficult to detect by palpation or mammography. In most cases, these “occult” primary tumors can now be detected by imaging studies using ultrasound or MRI.

All types of invasive carcinoma are graded using the Nottingham Histologic Score. Carcinomas are scored for tubule formation, nuclear pleomorphism, and mitotic rate and the points added to divide carcinomas into grade I (well differentiated), grade II (moderately differentiated), and grade III (poorly differentiated) types. **Grade I** carcinomas grow in a tubular pattern with small round nuclei and have a low proliferative rate (Fig. 23-23A). **Grade II** carcinomas may also show some tubule formation, but solid clusters or single infiltrating cells are also present. There is a greater degree of nuclear pleomorphism and mitotic figures are present (Fig. 23-23B). **Grade III** carcinomas invade as ragged nests or solid sheets of cells with enlarged irregular nuclei. A high proliferative rate and areas of tumor necrosis are common (Fig. 23-23C).

ER-positive, HER2-negative carcinoma. Many morphologic patterns are possible, with grades ranging from well to poorly differentiated. Essentially all well differentiated carcinomas are in this group. Mucinous, papillary, cribriform, and lobular patterns may be present and may be so prominent as to prompt classification as a special histologic type (described later).

HER2-positive carcinoma. The majority of these carcinomas are poorly differentiated with only a few classified as moderately differentiated. There is no specific morphologic pattern associated with this cell type. About 50% of apocrine carcinomas and 40% of micropapillary carcinomas (described later) are in this group. The associated DCIS is often more extensive than that associated with other types of invasive carcinoma.

ER-negative, HER2-negative carcinomas. Almost all of these tumors are poorly differentiated and several typical histologic patterns are recognized. Many have circumscribed pushing borders with a central fibrotic or necrotic center. Others have a similar appearance but with a prominent lymphocytic infiltrate and fall into the group of “carcinomas with medullary features” (described later). Spindle cell, squamous, and matrix producing patterns can also be seen. DCIS is generally very limited or not present.

Special Histologic Types of Invasive Carcinoma

Multiple subtypes of invasive carcinoma are recognized with distinctive morphologies and relatively unique biologic characteristics. Like breast cancers of “no special type,” these special tumors can be organized into groups based on expression of ER and HER2, which carry their usual therapeutic implications. However, special histologic types of breast cancer often harbor unique genetic aberrations, sometimes have distinct gene signatures, and frequently show associations with clinical behavior and prognosis that break the “rules” that have been established for breast cancers of no special type. Although relatively uncommon, study of these tumors has also provided important insights into breast cancer pathogenesis, some of which merit brief discussion.